

December 2010

NIEHS Spotlight



[Birnbaum leads NIEHS delegation at APHA](#)

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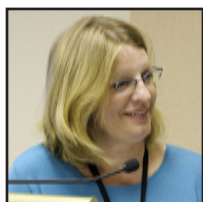
[WETP gets "back to basics"](#)

More than 100 NIEHS awardees and representatives from federal agencies, labor unions, and nonprofit organizations got "back to basics" at the Worker Education and Training Program fall meeting.



[Former trainee leads APHA session on climate change](#)

Epidemiologist Rose Ramos, Ph.D., organized and moderated a session that examined the implications of climate change on public health, especially in urban areas.



[Gray and Lawler attend children's environmental health symposium](#)

Two representatives from NIEHS recently attended a symposium that focused on the effects of environmental toxins on early life development.



[Training grant directors meet at NIEHS](#)

Directors of the Ruth L. Kirschstein National Research Service Award Institutional Research Training Grants met at NIEHS recently to discuss updates to the program.

Science Notebook



[Researchers honored at Science Awards Day](#)

NIEHS Intramural scientists and trainees stepped away from their laboratories and devoted the day to recognizing the scientific achievements of their colleagues and peers.



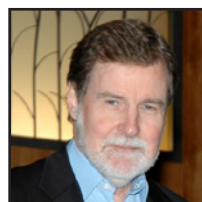
[Researchers meet to kick off nano consortium](#)

Researchers from the newly funded NIEHS nanotechnology centers gathered to introduce their projects and to stimulate coordination and collaboration among scientists.



[Nel delivers nano lecture](#)

Understanding how nanomaterials interact with biological systems is essential to ensure their safe use, according to NIEHS grantee Andre Nel, M.D., Ph.D.



[Environmental Mutagen Society highlights Wilson's research](#)

The 41st annual meeting of the Environmental Mutagen Society (EMS) Oct. 23-27 in Fort Worth showcased the importance of NIEHS to the environmental health community.



[NIEHS hosts workshop on gut microbiome](#)

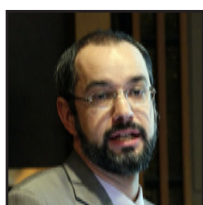
With its latest state-of-the-science workshop Nov. 17-18, the NIEHS took a proactive step forward to promote an exciting new area of research in environmental health science.

NIEHS Spotlight



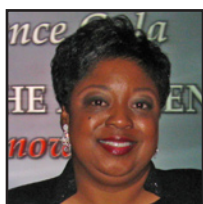
[Breast cancer and the environment program expanding](#)

The annual meeting of the Breast Cancer and the Environment Research Program marked the successes and expansion of the transdisciplinary program.



[NIEHS program featured at mHealth Summit](#)

The NIEHS-led Exposure Biology Program was highlighted at a meeting on the use of mobile devices in health care and personal exposure monitoring.



[Packenham shines at STEM conference](#)

NIEHS scientist Joan Packenham, Ph.D., was honored Oct. 30 at the 15th annual Women of Color STEM Conference in Dallas for her achievements in the sciences.



[NTP scientists earn prestigious toxicology certification](#)

Four more NTP scientists made an important advance in toxicology's professional ranks by satisfying requirements for American Board of Toxicology certification.



[NIEHS ethics counselor wins NIH mentoring award](#)

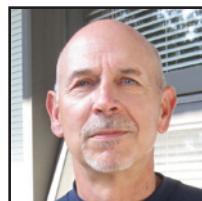
Bruce Androphy, J.D., received a Workforce Recruitment Program award at the NIH 2010 Disability Employment Awareness Month observance and awards program Oct. 28.



[Superfund film raises awareness of well water arsenic](#) Video

The short film "In Small Doses" draws attention to the high levels of naturally occurring arsenic and is an effective way to spread the message to a large audience.

Science Notebook



[Superfund researchers propose exposome paradigm](#)

The article presents a compelling argument for a fundamental — and possibly controversial — change in the way epidemiologists measure environmental exposure.



[Adelman links chromatin architecture and gene regulation](#)

NIEHS investigator Karen Adelman, Ph.D., and several other Institute researchers wanted to understand how a cell differentially regulates two types of genes.



[Whole genome sequencing illuminates lagging strand DNA replication](#)

New research led by NIEHS Principal Investigator Thomas Kunkel, Ph.D., may provide the answer to a decades-old question about the fundamentals of DNA replication..



[This month in EHP](#)

The December issue of Environmental Health Perspectives (EHP) heats up with the feature news article "A Closer Look at Climate Change Skepticism."



[Upcoming distinguished lecture by Haifan Lin](#)

Lin will present his research findings in a lecture Dec. 14 titled "A Novel Small RNA-Mediated Epigenetic Mechanism Related to Stem Cells."

NIEHS Spotlight



[Interdisciplinary experience leads to academic position](#)

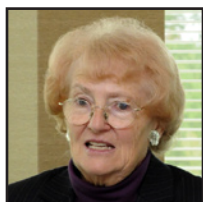
Rebecca Heise, Ph.D., a former trainee at NIEHS, is taking the next step in her scientific career as a tenure-track assistant professor at Virginia Commonwealth University.



[Dartmouth researcher receives Superfund award](#)

Courtney Kozul-Horvath, Ph.D., became the thirteenth recipient of the annual Karen Wetterhahn Memorial Award on Nov. 12 at the Superfund Annual Meeting.

Inside the Institute



[Seminar explores multiple chemical sensitivities topic](#)

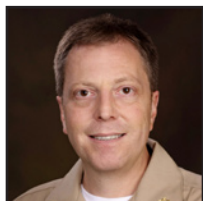


An Oct. 27 guest lecture at NIEHS trained the spotlight on growing concerns about the environmentally triggered disability Multiple Chemical Sensitivities (MCS).



[NIEHS celebrates Native American Heritage Month](#)

NIEHS celebrated Native American heritage this year with a lively program sponsored by the Institute's Diversity Council and the Haliwa-Saponi Indian Tribe of North Carolina.



[News from up north – the Bethesda office](#)

The newly rejuvenated NIEHS Bethesda office is approaching the celebration of its first full year of operation, its full complement of staff, and a long list of accomplishments.

Extramural Research

[Extramural papers of the month](#)

- [Death rates climb during heat waves](#)
- [Sequencing the exposome](#)
- [Epigenetic changes and low-dose BPA in breast epithelial cells](#)
- [Genetic driver of severe allergic asthma](#)

Intramural Research

[Intramural papers of the month](#)

- [Succimer treatment shows limited efficacy at reducing organic mercury in children](#)
- [Releasing the brake on synaptic plasticity](#)
- [mtDNA helicase mutants differ biochemically](#)
- [Gender differences in glucocorticoid-mediated inflammation](#)

Calendar of Upcoming Events

- **Dec. 6** in Rodbell Auditorium, 10:00-11:30 a.m. — Keystone Science Lecture Seminar Series with Irva Hertz-Picciotto, Ph.D., presenting “An Update on Environment and Autism: Findings from the CHARGE Study”
- **Dec. 7** in Executive Conference Room, 12:00-1:00 p.m. — Receptor Mechanisms Discussion Group with William J. Zuercher, Ph.D., speaking on “Open Access Chemical Probes for Drug Discovery”
- **Dec. 9** in Rall D-450, 10:00-11:30 a.m. — Laboratory of Molecular Carcinogenesis Seminar Series talk on “Epigenetic Regulation in Embryonic Stem Cells,” by Barbara Panning, Ph.D.
- **Dec. 10** in Rodbell Auditorium, 10:00-11:30 a.m. — Laboratory of Molecular Genetics Fellows Invited Seminar Series, featuring Robert Crouch, Ph.D., exploring “Ribonucleases H: Substrates *in vitro* and Effects of Loss *in vivo*”
- **Dec. 14** in Rodbell Auditorium, 11:00-12:30 p.m. — Distinguished Lecture Series presentation by Haifan Lin, Ph.D., exploring “A Novel Small-RNA Mediated Epigenetic Mechanism Related to Stem Cells”
- **Dec. 15** online, 2:30-3:30 p.m. — Superfund Research Program Funding Opportunities, http://clu-in.org/live/#Superfund_Research_Program_Funding_Opportunities_20101215
- **Dec. 16** in Rall D-450, 10:00-11:00 a.m. — Susan Henning, Ph.D., exploring “The Elusive Intestinal Stem Cell: Progress and Challenges” as part of the Laboratory of Molecular Carcinogenesis Seminar Series
- **Dec. 16** in Rodbell Auditorium, 1:00-3:00 p.m. — 2010 Director’s Awards Ceremony and International Festival
- View More Events: [NIEHS Public Calendar](#)


NIEHS Spotlight

Birnbaum leads NIEHS delegation at APHA

By Ernie Hood

The American Public Health Association (APHA) annual meeting has long been an important event on the NIEHS calendar, but with this year's theme of "Social Justice: A Public Health Imperative," the November 6-10 [gathering](#) in Denver was particularly significant for the Institute.







Linked video:

[Watch opening video from the APHA annual meeting \(3:50\)](#)

(Launches in new window)

Download Media Player:  Flash 

"We were a major presence at APHA this year — even more so than usual," said NIEHS/NTP Director Linda Birnbaum, Ph.D. "From our history of pioneering research in environmental justice to our current focus on the intersection of public health and climate change, NIEHS has a long tradition of building effective linkages among researchers, community groups, and residents to improve public health and reduce health disparities. So we were excited to have the opportunity to showcase our efforts and our commitment to social justice at the Denver meeting" ([see text box](#)).



Shown standing before the popular NIEHS/EHP exhibit, Birnbaum enjoyed a visit with her son, Bernard "Bernie" Birnbaum, M.D., left. He is a faculty member at a family medicine physician resident program in nearby Ft. Collins, Colo., with research interests in community medicine and the care of the underserved. (Photo courtesy Christine Flowers)

In addition to Birnbaum, many NIEHS representatives moderated sessions or gave presentations at the conference, including major sessions on environmental justice and health, green jobs, the National Children's Study, and more. An estimated 12,000 public health professionals from around the world attended the conference, which featured more than 1,000 scientific sessions highlighting the latest public health research and advocacy, and reflecting the broad impact of the field on the lives of U.S. families.

Birnbaum delivered two major presentations at the meeting. The first, "Using Science to Promote Environmental and Climate Justice: The NIEHS Perspective," directly addressed the meeting's emphasis on social justice and public health. She described the long-standing NIEHS commitment to environmental justice, the 2007 establishment of the Partnerships for Environmental Public Health program, the contributions of environmental health research to environmental justice and efforts to combat health disparities, and the current initiatives addressing climate change and human health, particularly as they pertain to vulnerable populations.

As part of a Vietnam Caucus session exploring health issues following the Vietnam War, Birnbaum explored "Health Consequences of Dioxins in Humans." As she explained, the persistent organic pollutants known as

dioxins include the Vietnam War-era herbicide Agent Orange and several other highly toxic chemicals. They are human carcinogens, and exposures can also result in a plethora of non-cancer effects such as type II diabetes, endometriosis, and a variety of developmental problems, with the embryo and fetus being especially vulnerable.

Research has shown that everyone has some exposure to dioxins, and that adverse health effects may be occurring in the high end of the general population's exposure levels. The best public health approach, said Birnbaum, is to decrease exposures by continuing to reduce sources and environmental levels of dioxins.

Next year's APHA meeting, which will be its 139th Annual Meeting and Exposition, will be held in Washington, D.C., Oct. 29–Nov. 2. With its theme, "Healthy Communities Promote Healthy Minds and Bodies," no doubt NIEHS and its delegation will again make substantial contributions to the proceedings.

(Ernie Hood is a contract writer for the NIEHS Office of Communications and Public Liaison.)



Left to right, EHP contractor Dana McNally, NIEHS Director of Communications and Public Liaison Christine Flowers, and EHP Managing Editor Rita Hanson welcome visitors to the exhibit. (Photo courtesy of Christine Flowers)

NIEHS at the 2010 APHA Annual Meeting

Environmental Justice and Health Forum — Presenter: Liam O'Fallon, Workshop Facilitators: Gwen Collman, Ph.D., John Balbus, M.D.

Innovations in International Health — Presenters: Janet Archer, Fikri Yucel, Mwenda Kudumu, Pamela Schwingl, Ph.D., and M.S. Bornman, with Social and Scientific Systems Inc., contractor for the NIEHS Sister Study

Blue/Green #1: Producing Green and Working Safe — Presenter: Sharon Beard

Blue/Green #2: Making Green Jobs Safe Jobs — Presenter: Joseph (Chip) Hughes

Minority Health Research — Presenter: Michelle Sever, Ph.D.

Climate Change and Public Health: Research, Communication and Mitigation Activities at the International, Federal, Local, and Personal Levels — Presenter: John Balbus, M.D.

Improving Environmental Health and Occupational Safety and Health Through Training Programs, Capacity Building, Partnerships, and Public Health Education — Organizer and Moderator: Allen Dearry, Ph.D.

Partnering With Communities to Address Environmental and Occupational Justice Concerns — Organizer and Moderator: Liam O'Fallon

Partners in Research: Strengthening and Evaluating Models for Equitable Participation in Environmental Public Health Research and Action — Organizer and Moderator: Liam O'Fallon

National Children's Study: How Environment Affects Child Health — Organizer, Moderator, and Presenter: Allen Dearry, Ph.D.

WETP gets “back to basics”

By Daniel Youhas

More than 100 NIEHS awardees and representatives from federal agencies, labor unions, and nonprofit organizations got “back to basics” at the NIEHS [Worker Education and Training \(WETP\)](#) Fall Awardee and Technical Meeting in Research Triangle Park, N.C. Oct. 25-26 to discuss new and emerging worker education and training issues related to hazardous waste cleanup, the green economy, and environmental justice.

Created in 1986 under the Superfund Amendments and Reauthorization Act (SARA), WETP funds non-profit organizations with a demonstrated track record in developing and delivering hazardous waste operation and emergency responder (HAZWOPER) training under the standards implemented by the U.S. Department of Labor Occupational Safety and Health Administration (OSHA).

In October 2010, NIEHS announced grant awards of \$36 million to 20 organizations to develop safety and health training for workers involved in hazardous waste operations and transportation, environmental restoration of contaminated facilities, and chemical emergency response ([see story](#)). Several of the new awardees shared insights into their training for additional target groups, such as veterans with disabilities, maritime workers, and utility workers.

WETP Director Joseph “Chip” Hughes opened the two-day meeting by highlighting the WETP program and awardee achievements over the past 5 years, including providing safety and health training for first responders to Hurricane Katrina, the Haiti earthquake, and Gulf oil spill.

“The fall 2008 workshop focused on safety and health in the green economy and that was a good start,” Hughes said. “However, we need to continue promoting the safety and health of workers in the greening economy, especially as it relates to nanotechnology.” Rice University chemist [Kristen Kulinowski, Ph.D.](#), and Environmental Profiles, Inc. Senior Consultant [Bruce Lippy, Ph.D.](#), past [NIEHS meeting panelists](#), are drafting a paper that will provide a framework for WETP awardees to train their constituents about the hazards of and controls for specific nanomaterials in their workplaces.

Deborah Berkowitz, OSHA chief of staff, highlighted the OSHA/WETP minimum criteria document for OSHA’s Susan Harwood Training Grant Program, developing the April 2010 National Action Summit for Latino Worker Health and Safety, and OSHA’s role during the Gulf oil spill.



Hughes, above, welcomed the diverse group of grantees and partners to the fall meeting. He and his staff make sure the meetings address the latest developments in worker training and safety. (Photo courtesy of Steve McCaw)



Grantees filled the NIEHS auditorium to capacity for the two-day workshop. (Photo courtesy of Steve McCaw)

Gwen Collman, Ph.D., NIEHS Division of Extramural Research and Training (DERT) interim director, announced a new health study for oil spill cleanup workers and volunteers. Collman told the audience, “We do not have good science that connects environmental [toxin] levels to personal levels. The body handles exposures in different ways.” NIEHS expects 27,000 people will participate in NIEHS-funded research to assess short and long-term mental and physical health effects.

In conjunction with the study, NIEHS announced a Request for Applications to study the health, environmental and economic effects of the Gulf oil spill. The agency plans to utilize community organizations to establish the evidence base needed to inform recovery and develop strategies to promote health and well-being of populations.

Other panels discussed WETP involvement in the April 2010 [Liberty RadEx](#) homeland security simulation exercise, promoting 10 CFR Part 851 Worker Safety and Health Program throughout the Department of Energy (DOE) complex, Environmental Training and Environmental Justice, and the White House’s Council on Environmental Quality recovery through home retrofitting program.

The next WETP awardee and technical workshop is scheduled for Spring 2011.

(Daniel Youhas is a contractor for the NIEHS Superfund Research Program and WETP.)

Remembering the aftermath of the World Trade Center attack

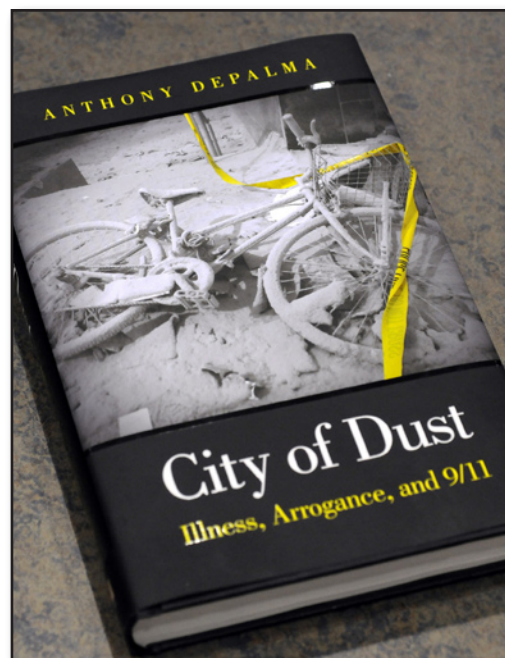
During lunch, author Anthony DePalma, a former New York Times reporter, presented a dramatic overview of his new book, *City of Dust: Illness, Arrogance, and 9/11*.

Beginning with a call from NIEHS to Paul Liroy, Ph.D., at the University of Medicine and Dentistry of New Jersey Health Center soon after the 9/11 attacks, the book is an examination of the health crisis that followed from the poisonous dusting of New York City in the aftermath of the World Trade Center disaster. According to DePalma, near the epicenter the dust was as much as four inches thick.

DePalma recounts the stories of a number who died from complications linked to the dust, as well as of some who are still alive but continue to experience severe respiratory and other ailments.



Representing OSHA, Berkowitz described activities involving her agency and WETP. OSHA is one of several partner agencies working with WETP to promote worker safety. (Photo courtesy of Steve McCaw)



DePalma’s presentation was the latest in a series of talks by authors with ties to WETP on the social, economic, and safety issues facing workers exposed to hazards on the job. (Photo courtesy of Steve McCaw)

Former trainee leads APHA session on climate change

By Eddy Ball

As part of the 2010 annual meeting of the American Public Health Association (APHA), epidemiologist Rose Ramos, Ph.D., a former NIEHS trainee, organized and moderated a session Nov. 9 that combined her interests in environmental public health with her experiences from 2005 to 2008 as the Institute's NIH Health Disparities Fellow.

The session examined the implications of climate change on public health and brought home the message that global health concerns are very clearly domestic health concerns as well.

"It's evident that urban governments are not prepared for what could be a dramatic increase in heat-related morbidity and mortality, especially among currently underserved populations," Ramos explained. "I hope that continued studies can help public health advocates understand the pressing need to prepare for the effects of climate change."

As Ramos said afterwards, the presentations were very well received by an engaged audience that included her former mentor, NIEHS Director Emeritus Ken Olden, Ph.D., and NIEHS Senior Advisor for Public Health John Balbus, M.D. ([see text box](#)).



Unlike most trainees at NIEHS, Ramos didn't spend her fellowship at the bench. Rather, she considered the urban landscape her laboratory and saw policy forums as the venues for sharing much of her research. (Photo courtesy of Steve McCaw)

An urban focus on climate change

Titled "[Summer in the city: Addressing health impacts and disparities posed by urban heat events](#)," Ramos' session explored the greater mortality associated with extreme heat and air pollution episodes in sprawling metropolitan areas, with a focus on larger cities in the U.S. The four presenters examined climate and health data from major urban areas, largely in the U.S., with the goal of discovering useful tools for local public health departments to target increasingly scarce resources for preventing adverse health outcomes due to heat waves.

The presenters explored several aspects of this growing public health issue:

- Natalie Sampson — [Reducing social disparities of heatwave impacts in a changing climate: A qualitative investigation of heat planning in four U.S. cities](#)
- Colleen Reid — [Climate change, heat waves, and population vulnerability: Using the environmental public health tracking network for validity testing of the heat vulnerability index](#)
- Vivek Shandas, Ph.D. — [Climate justice: Assessing the spatial distribution of urban heat island impacts on populations living in the United States](#)
- Brian Stone, Ph.D. — [Are residents of sprawling metropolitan regions more vulnerable to climate-induced health effects?](#)

While at NIEHS, Ramos and Olden published the first study to examine disparities in the prevalence of metabolic syndrome among U.S. females of childbearing age. After leaving NIEHS, Ramos worked on a diabetes surveillance project for the City of San Antonio. During this time, a correlation had been observed between the city's heat waves and an increase in diabetes-related complications resulting in hospitalization. Ramos is currently a research fellow at the University of Pittsburgh where she completed graduate school.

NIEHS participates in sessions on climate change

As well as attending the session led by Ramos, NIEHS Senior Advisor for Public Health John Balbus, M.D. organized two sessions and spoke in a third one at the APHA meeting.

The first was a special plenary session of the APHA that was entitled "[Federal Perspectives on Social Justice, Climate Change and Environmental Health](#)." NIEHS/NTP Director Linda Birnbaum, Ph.D. was the first speaker of the session. She was joined by Irene Dankwa-Mullan, M.D., of the National Institute on Minority Health and Health Disparities, and Onyemaechi Nweke, Dr.P.H., of the U.S. Environmental Protection Agency's Office of Environmental Justice.

The second was an informational and listening session for the U.S. Global Change Research Program organized and moderated by Balbus, with a focus on the Interagency Group on Climate Change and Human Health and other climate change and human health activities of the federal government. George Luber, Ph.D., of the Centers for Disease Control and Prevention, and Tanya Maslak of the U.S. Global Change Research Program were the other speakers. About 40 people attended and engaged in a spirited question-and-answer session following the three presentations.

The third was a scientific session on [Climate change and public health: Research, communication, and mitigation activities at the international, federal, local, and personal levels](#) organized by Oregon State Environmental Public Health Administrator Gail Shibley, J.D. Balbus was one of three speakers, giving a talk on federal activities related to climate change and public health, with an emphasis on the new research funding opportunities at NIEHS and NIH and the development of the human health impacts of climate change program at NIEHS. Other speakers included Luber and Gregg Thomas of the Department of Environmental Health, City and County of Denver.

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Gray and Lawler attend children's environmental health symposium

By Robin Arnette

Since children's health research is one of the top priorities for NIEHS, two scientists from the Division of Extramural Research and Training (DERT) recently attended a symposium that focused on the affects of environmental toxins on early life development.

Kimberly Gray, Ph.D., and Cindy Lawler, Ph.D., both scientific program administrators for the [NIEHS Centers for Children's Environmental Health and Disease Prevention Research](#), participated in panel discussions at the Sixth Biennial Scientific Symposium sponsored by the [Children's Environmental Health Institute](#). Held Oct. 21-22 at the Space Center Houston in Texas, the symposium titled "Prenatal and Early Life Exposures: How Environmental Toxins Affect the Course of Childhood" addressed the competing roles of genetic and environmental factors in the causation of childhood diseases.

Gray served on a government perspective panel titled “Early Life Exposure: The Search for Cause and Effect, from the Laboratory to Surveillance.” She and other panel participants discussed several topics, such as how the National Environmental Public Health Tracking (EPHT) Network protects communities from adverse health effects; the level of cooperation between NASA, the CDC, and the Agency for Toxic Substances and Disease Registry (ATSDR) in monitoring environmental public health; how the NIEHS Centers for Children’s Environmental Health and Disease Prevention translates its findings to clinical and public health professionals and policy makers; and the purpose and benefits of the National Children’s Study.

“I really enjoyed [the panel],” Gray said. “Participants appeared engaged and interested in learning more about the science because they asked good questions.”

Gray stressed that the goals of the NIEHS children’s environmental health centers are to “stimulate research on the role of environment in the etiology of disease/dysfunction among children, develop novel effective intervention and prevention strategies, and promote the translation of basic research into applied intervention and prevention methods.” However, disseminating information about the research is the center’s main objective, when she and other center representatives attend professional meetings.

Lawler’s panel was titled “The Role of Environmental Factors in the Etiology of Autism Spectrum Disorder,” and the discussions centered on why autism is the fastest growing developmental disability in the United States and how toxins and other environmental triggers may contribute to the pathophysiology of the disorder.

Lawler explained that autism or autism spectrum disorder (ASD) is a group of complex neurodevelopmental syndromes that are diagnosed by impairments in communication and social interaction, along with restrictive patterns of behavior or interest. The Institute’s [Autism](#) Web page details the variety of research that NIEHS supports.

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*Gray oversees the extramural grant portfolio on perinatal and pediatric epidemiology.
(Photo courtesy of Steve McCaw)*



*Lawler oversees the extramural grant portfolio on autism and autism spectrum disorders.
(Photo courtesy of Steve McCaw)*

Training grant directors meet at NIEHS

By Robin Arnette

Directors of the Ruth L. Kirschstein National Research Service Award (NRSA) Institutional Research Training Grants (T32) met at NIEHS recently to discuss updates to the program. Carol Shreffler, Ph.D., program director for training and career development at NIEHS, chaired the Nov. 3 meeting and provided introductions for the day's speakers.

NIEHS/NTP Director Linda Birnbaum, Ph.D., welcomed the attendees and gave the first presentation of the day — an overview of the ongoing research at the Institute. She said that NIEHS uses environmental sciences to understand human disease, but emphasized that public health was the common denominator for all of the divisions of NIEHS, including the Office of the Director, Division of Extramural Research and Training (DERT), Division of Intramural Research (DIR), National Toxicology Program (NTP), and Environmental Health Perspectives (EHP), the scientific journal published by NIEHS.

“Standard biomedical research is focused on the idea of ‘bench to bedside,’ but the mission of NIEHS focuses on ‘bench to public health and prevention,’” Birnbaum maintained. “Our mission is one of the most ambitious missions of all the Institutes of the NIH. It’s a challenge that I know we can tackle.”

Gwen Collman, Ph.D., acting director of DERT, communicated information about funding opportunity announcements (FOAs) involving NIEHS, training opportunities in environmental public health, and several upcoming DERT workshops.

Next on the program agenda was the Chief of the NIEHS Program Analysis Branch Christie Drew, Ph.D. Drew outlined the development of CareerTrac, a trainee tracking system that will provide career outcome data for the more than 5,000 extramural trainees. The program, expected to go live in 2011, builds upon a prototype created by the Fogarty International Center. According to Drew, CareerTrac “will provide a sense of trainee outcomes — where they work, what they have accomplished, what areas of science they are working in, etc.” Additionally, CareerTrac will assist Training Directors by saving trainee data from year to year and facilitating the production of key tables for their renewal applications and progress reports.

Several other speakers participated in the meeting including Paul Watkins, M.D., University of North Carolina at Chapel Hill; Rodney Ulane, Ph.D., NIH; Harold Pincus, M.D., Columbia University; Charles Epstein, M.D., The Broad Institute of Harvard and MIT; and Astrid Haugen and Liam O’Fallon, both of NIEHS.



In her overview to the meeting participants, Birnbaum touted the Institute's role in the recent Gulf oil spill. "NIEHS was one of the first agencies to respond to the Deepwater Horizon oil spill, with staff on the ground days after the explosion to provide worker safety training for the cleanup," said Birnbaum. (Photo courtesy of Steve McCaw)



Gwen Collman (Photo courtesy of Steve McCaw)

Concerns for the future of the biomedical workforce

In his presentation, Ulane highlighted the variety of NIH grants available for individuals to participate in biomedical research — everything from pre-baccalaureate to senior scientists. However, he mentioned that a number of circumstances contribute to the erosion of enthusiasm for a research career in biomedical science.

He said that for the past three years, the hiring of tenure-track faculty has not kept pace with the previous year, and the number of new and competing research program (R01) grant awards has remained essentially static at 10,000 per year since 2000.

“Yet, the total number of students enrolled in biomedical science Ph.D. programs has increased approximately 40 percent from 2000 to 2008,” Ulane added. “It’s not hard to see why the large number of postdocs waiting to enter tenure-track positions may wonder if they will ever get a chance to lead their own lab.”

Ulane said that the biomedical research community could reverse this trend by hiring more tenure-track faculty and increasing the number of R01s. It could also boost the number of researchers by retaining more clinician and physician scientists and studying how and when to initiate inter-, cross-, and trans-disciplinary training.



*Shreffler made sure that the NRSA meeting ran smoothly.
(Photo courtesy of Steve McCaw)*



Epstein serves as the program manager for epigenomics at The Broad Institute of Harvard and MIT. He highlighted the innovations that his epigenomics mapping center has made since its inception. (Photo courtesy of Steve McCaw)



O'Fallon, program analyst for Partnerships for Environmental Public Health (PEHP), explained what the PEHP does and relayed future program initiatives. (Photo courtesy of Steve McCaw)

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Breast cancer and the environment program expanding

By Matt Goad

The annual meeting of the Breast Cancer and the Environment Research program (BCERP) Nov. 16-18 in New York marked the successes and expansion of the transdisciplinary program.

Les Reinlib, Ph.D., the program administrator at the NIEHS Susceptibility and Population Health Branch (SPHB), said the BCERP is moving into a second phase that will expand the research goals to look at risk factors for breast cancer over a lifetime. Research suggests that there are windows of susceptibility — *in utero*, puberty, pregnancy and post-menopausal stages of life — when women are particularly vulnerable to environmental causes of breast cancer. Phase one of the BCERP has focused only on puberty.



“We’re now in the trajectory to expand the program,” Reinlib said, “so that we can understand over the lifetime of a woman what are the windows of susceptibility when one needs to be especially careful concerning exposures that might need to be avoided for breast cancer risk.”

Also representing NIEHS at the meeting were NIEHS/NTP Director Linda Birnbaum, Ph.D., who gave opening remarks; Gwen Coleman, Ph.D., director for the Division of Extramural Research and Training; Claudia Thompson, Ph.D., SPHB acting chief; Dale Sandler, Ph.D., Epidemiology Branch chief and principal investigator on the NIEHS Sister Study; and several others.

The BCERP is a network of centers created in 2003 by NIEHS and the National Cancer Institute. Phase two of the program features increased numbers of investigators and community partners around the nation and a re-organized advisory committee that represents scientific expertise and the breast cancer survivor and advocacy community.

An ambitious study by six University of California campuses, for example, will follow 150,000 women for 50 years. Other studies will focus on the pregnancy window.

Studies of the environmental influences on early onset of puberty in young girls – an established risk factor for future breast cancer – will continue, as well.

There are some factors affected by the environment, such as obesity, for example, that common sense says would affect health, Reinlib said, but in a time when there are so many artificial chemicals in the environment, it is harder to tell what breast cancer risks women face.

Reinlib pointed to recent questions about bottled water.

“Who would have imagined that a bottle of spring water could actually affect your health?” Reinlib continued. “And yet now we are finding out that the bottles may contain chemicals such as phthalates that could leach out, to a small, but measurable extent, and are found in our bodies.”

Reports are already pointing to weak relationships between exposure to these endocrine disruptors and the early onset of puberty. This factor may be one of the pieces in the complex puzzle that alters risk of breast cancer. Further studies are under way within the BCERP to understand the impact of indoor pesticides, heavy metals, diet, pregnancy, and hormone-like substances found in cosmetics and sunscreen.

Presentations from the public portion of the BCERP annual meeting will soon be available on the [BCERP](#) website.

(Matt Goad is a contract writer with the NIEHS Office of Communications and Public Liaison.)

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NIEHS program featured at mHealth Summit

By L.H. Lazarus and Matt Goad

The NIEHS-led Exposure Biology Program was highlighted at the second annual [mHealth Summit](#) Nov. 8-10 in Washington, D.C., where health care professionals and researchers gathered to discuss the use of mobile devices in health care, as well as their application in personal exposure monitoring currently being explored by grantees supported by NIEHS and other NIH institutes and centers.

The NIH, Foundation for the NIH, and mHealth Alliance were event partners. Sponsors included a range of non-profits, associations, and corporations with interests in health care and mobile communication.

Exposure biology

The Exposure Biology Program, part of the NIH Genes Environment, and Health Initiative (GEI), funds grants for the development of innovative technologies to monitor the personal environment and the individual response to exposure. The initiative includes tools to determine environmental exposure to various chemicals, diet, physical activity, and psychosocial stress, as well as identify specific changes in the body's response to these factors.

In his opening address at the conference, NIH Director Francis Collins, M.D., Ph.D., stressed the importance of NIEHS in the NIH GEI and gave examples of how these tools can change the health care enterprise.

The four distinguished keynote speakers included Microsoft founder and philanthropist Bill Gates, who discussed the focus of the Bill & Melinda Gates Foundation on emerging global health issues that combine evolving technologies with new advances in biology and medicine. The foundation is a major donor to the GEI effort.

David Balshaw, Ph.D., program administrator for the NIEHS Division of Extramural Research and Training (DERT), attended the summit as a member of the organizing committee.

Cell phones and health care

"The major themes of the meeting," Balshaw explained, "included the discussion of practical implications of building an mHealth enterprise." Primary concerns involved security and privacy protection with a focus on state of the science and realities of what can and cannot be done today, as well as developing strategies to enhance the adaptation of mobile technologies in health care practice, he said.



Shown at an earlier meeting at NIEHS on systems biology, Balshaw oversees grants funding research at the intersection of technical advances and the environmental health sciences. (Photo courtesy of Steve McCaw)

Balshaw noted that there are 4.5 billion cell phones currently in use among the 6.5 billion people on the planet and that these numbers indicate cell phones are rapidly becoming a primary means of communication, especially in developing nations with a limited landline network. In many countries, mobile communication may be the only link to the outside world.

Unobtrusive monitoring devices utilizing cell phone technology have the potential to readily identify environmental exposures to agriculture pesticides and industrial wastes in the most vulnerable populations, such as children and farmers, and maintain open communication between patients and a distant health care provider.

As an example of mobile communication in prevention and treatment, Balshaw pointed to cell phones as an integral component in the text-for-baby program which makes vital information on infant care available to young mothers. This service consists of free texts on medical data, including reminders on baby health services, such as vaccination schedules and routine health checkups.

The NIEHS perspective on mHealth

Balshaw noted that, as it is currently implemented, mHealth focuses largely on clinical applications of technology for monitoring physiological parameters, patient compliance, and delivery of health-related information to patients. However, with the increased power and acceptance of wireless technologies and the development of new sensor systems, such as wearable chemical sensors enabling constant and immediate feedback about possible environmental influences on health, it becomes increasingly feasible to incorporate more information into clinical decision-making.

The use of wireless devices also enhances privacy and security. These are issues in countries lacking reliable means of communication and for research involving human subjects. In addition, the instant monitoring and messaging availability of cell phones becomes critical component in emergency situations.

(Matt Goad is a contract writer with the NIEHS Office of Communications and Public Liaison.)

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Packenham shines at STEM conference

By Matt Goad

NIEHS scientist Joan Packenham, Ph.D., was honored Oct. 30 at the 15th annual Women of Color STEM (Science, Technology, Engineering, and Mathematics) Conference in Dallas for her years of work and achievements in the sciences. In her talk and interaction at the conference, Packenham also promoted career and training opportunities in the environmental health sciences.

Packenham, director of the Institute's Office of Human Research Compliance (OHRC), attended the three-day conference, capped by the 15th Women of Color STEM Awards Gala, a black-tie event where she received her award for STEM career achievement in government.

"The conference was exceptional," Packenham said. "It was great to see so many phenomenal women together who have made great contributions in STEM. Rarely do women scientists have an opportunity to interact and network with so many peers and role models in one place. It was an incredible experience."

The 28 awardees were of several different ethnicities, including African-American, Native American, Middle Eastern, Asian, Southeast Asian, Pacific Islander, and Latina. They were selected from a competitive group of approximately 300 nominees for 14 STEM award categories.

In her speech, Packenham accepted the award in the memory of her parents, both educators in Durham, N.C. Her mother was an elementary school teacher, and her father, who started as a high school biology teacher, finished his career as the K-12 science and mathematics supervisor for the Durham public school system.

“They gave me my first educational foundation and instilled in me core values, confidence, and the importance of giving back to the community,” Packenham said. “It was my father who gave me that first foundation and love of science. It was an honor for me to dedicate it to them.”



Packenham, above, posed with her award for career achievement. “I enjoyed meeting women in other scientific disciplines and learning what challenges they had to overcome and how they successfully handled those challenges,” she said. (Photo courtesy of Joan Packenham)

Promoting NIEHS and the environmental health sciences

There were more than 2,000 STEM professionals who attended the conference from industry and government, Packenham said. In addition, there were 500-600 undergraduate students from 38 colleges and universities. She participated in professional development workshops with other STEM professionals on knowledge management, teamwork, team building, and communication strategies.

She also gave a presentation, “Environmental Health Science UNWRAPPED,” in two life sciences sessions for the students, giving students inside knowledge about NIH, NIEHS, and career opportunities in the environmental health sciences.

“Besides receiving the award, the best part for me was interacting with the students,” she said. “They were very inquisitive about the National Institutes of Health, the National Institute of Environmental Health Sciences and career opportunities in the environmental sciences. Many students had never been introduced to the environmental health sciences and, therefore, had not considered exploring environmental sciences as a career option. It was exciting to give them their first lesson.”

Packenham said she has received e-mails from students since the conference, inquiring about educational opportunities, summer internships, and employment opportunities at NIEHS.

“I think we should have a booth at their Career Fair Expo,” she said. “The top science students from the various universities and colleges are there. It is an excellent venue for NIEHS to recruit for the Summers of Discovery Program [summer internship opportunities] and for other educational opportunities.”

Edith Lee, protocol specialist for the OHRC, who accompanied Packenham to the conference, said Packenham is a visionary who knows how to get things done.

“She’s not going to do something unless it’s going to work, or at least has done the research to see that it is possible,” Lee said. “She knows what battles to fight and what battles to leave alone. I’ve known her about a decade, and she’s a very competent person.”

As director of the OHRC, Packenham oversees the NIEHS Human Research Protection Program, which protects the rights and welfare of human subjects by reviewing, approving, and monitoring clinical research activities involving human subjects within the Intramural Research Program.

(Matt Goad is a contract writer with the NIEHS Office of Communications and Public Liaison.)

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NTP scientists earn prestigious toxicology certification

By Eddy Ball

Four more National Toxicology Program (NTP) scientists made an important advance in toxicology's professional ranks by satisfying requirements for Diplomate of the American Board of Toxicology (D.A.B.T.) certification.

According to the organization, the certification is an international recognition of broad expertise in general toxicology for those with formal training in toxicology, as well as those trained in other related disciplines, often confers an advantage in the job market and career advancement, and is an objective demonstration of a toxicologist's breadth and currency of knowledge that supports scientific credibility.

The [American Board of Toxicology](#) officially certified the following NTP scientists as diplomates:

- [Chad Blystone, Ph.D.](#), of the NTP Toxicology Branch
- [Susan Elmore, D.V.M.](#), of the NTP Pathology Group
- [Gloria Jahnke, D.V.M.](#), of the NTP Report on Carcinogens Center
- [Mike Sanders, Ph.D.](#), of the NTP Program Operations Branch

In a message to the new diplomates, NIEHS/NTP Director Linda Birnbaum, Ph.D., who also holds D.A.B.T. certification, wrote, "Congratulations to all of you, and welcome to the team of outstanding diplomates at NTP." Speaking from experience, she added, "It's no mean feat to become a D.A.B.T., and your achievement is one more testament to the high caliber of science conducted by the NTP."

The American Board of Toxicology was established in 1979 to advance standards in the field of toxicology and to confer recognition upon those members of the profession who, measured against such standards, demonstrate competence. Certification requirements include a combination of education and experience, and a three-part examination.

Diplomates hold initial ABT certification for 5 years and must demonstrate that they actively practice toxicology, engage in continuing education, and maintain expert knowledge in their field prior to pursuing recertification.



Blystone is the lead on studies evaluating chemicals within the classes of parabens, phthalates, ethylene glycol ethers, and perfluoroalkyl acids. (Photo courtesy of Steve McCaw)



Elmore's expertise as a veterinary pathologist is critical in her group's oversight of NTP two-year rodent toxicology and carcinogenesis studies, which are recognized as the gold standard in the field. (Photo courtesy of Steve McCaw)



Jahnke has applied her scientific rigor in the preparation of the [12th Report on Carcinogens](#), which is nearing completion for final submission to the Secretary of the U.S. Department of Health and Human Services. (Photo courtesy of Steve McCaw)



As a lead scientist in the Chemical Metabolism and Disposition Workgroup, Sanders oversees research on absorption, distribution, metabolism, and excretion (ADME) as well as pharmacokinetics of xenobiotic materials of interest to the NTP. (Photo courtesy of Steve McCaw)

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NIEHS ethics counselor wins NIH mentoring award

By Emily Zhou

Director of the NIEHS Office of Ethics and Deputy Ethics Counselor [Bruce Androphy, J.D.](#), received a Workforce Recruitment Program award at the NIH 2010 Disability Employment Awareness Month observance and awards program Oct. 28. Androphy was recognized for his superior leadership in mentoring Tim Moore, a law student with a disability, last summer at NIEHS.

Moore, who attends the North Carolina Central University (NCCU) School of Law, worked on the forensics aspect of legal research, reviewed [Office of Government Ethics \(OGE\) SF-278](#) public disclosure reports, and improved online databases on the NIEHS intranet. He also learned about ethics law and helped with manuscript revision.

“Not only does your service establish NIH as an inclusive working environment,” said NIH Office of Equal Opportunity and Diversity Management Deputy Director [Hilda Dixon](#) of Androphy’s service, “but you also have offered both students and co-workers an encouragement to appreciate one another.”



Androphy is a key member of the NIEHS senior leadership team. Under his direction, the Institute has significantly expanded its ethics initiatives. See stories about Androphy and the Office of Ethics, since his appointment early this year, in the [January](#), [February](#), [May](#) and [July](#) issues of the Environmental Factor. (Photo courtesy of Steve McCaw)

Androphy said he really enjoyed the experience of working with a student with a disability very much and would certainly do it again. He praised Moore's outstanding work ethic.

Androphy was approached in the spring about whether he would supervise a second-year law school student from NCCU as a summer intern. During their interview, Moore impressed Androphy with his resume and maturity.

"We were short-staffed at the moment, and we thought he would be a great help for us," Androphy said.

Staff at NIEHS made the office entrance and other necessary equipment ready to accommodate Moore, who found NIEHS an extremely easy-access facility, as compared to facilities of other federal agencies. Moore told Androphy that NIEHS is one of the best places he has worked.

Androphy said that should the opportunity again be available, he would be happy to accommodate more legal interns in the future.

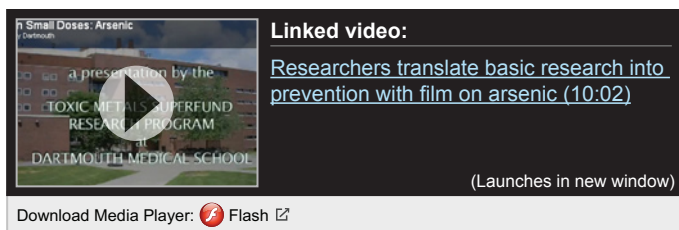
(Emily Zhou, Ph.D., is a research fellow in the NIEHS Laboratory of Signal Transduction Inositol Signaling Group.)

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Superfund film raises awareness of well water arsenic

By Angela Spivey

Dartmouth College's Superfund Research Program (SRP), funded by a grant from NIEHS, produced a film that is motivating homeowners in New Hampshire, Maine, and other parts of New England to test their private wells for arsenic contamination. Titled "In Small Doses: Arsenic," the short film draws attention to the high levels of naturally occurring arsenic in the area and is an effective way to spread the message to a large audience.



"What began as an idea to translate our research on the effects of low dose arsenic on the immune system became a highly successful communication tool with a specific message benefiting the private well community," said Laurie Rardin, who headed the effort. The Dartmouth SRP held screenings for the film at the NIEHS 2009 SRP Annual Meeting in New York City and at an independent theater in Concord, N.H. Rardin has also shown the film at meetings for well water experts, groundwater stakeholders and state health officials. She is pleased with the amount of publicity it has received. In addition, the film also appears on Dartmouth's website and YouTube.



Dartmouth SRP researcher Celia Chen, Ph.D., leads a team of Superfund researchers who are applying basic research in an effort to improve public health. (Photo courtesy of Michael Yacavone)

“There has been trickle-down coverage ever since the premiere, and the momentum is growing,” Rardin explained. “Several towns in New Hampshire are considering passing local ordinances requiring private well testing for arsenic, and many are showing the film on their local cable TV stations.” She adds, “We are addressing a specific community need, along with highlighting SRP research.”

Translating research into primary prevention

The film serves an important function because many well owners are not aware of the need to test for arsenic, which is odorless, tasteless, and not commonly thought of as a drinking water contaminant. According to Rardin, approximately 40 percent of the residents of New Hampshire use private wells as their source for household drinking water, but federal law does not require private well water testing.

As highlighted in the movie, Shari and Steve deYoung of Bow, N.H., purchased the \$15 test kit and learned that their well water contained arsenic levels higher than considered safe for long-term exposure. They resolved the problem by installing a simple, under-the-sink unit to remove the pollutant from their drinking water.



Rardin is working to ensure that as many citizens and public health specialists as possible become aware of arsenic in the region's groundwater. (Photo courtesy of Laurie Rardin)

Drinking water testing kits are available through state environmental agencies or health departments in all New England states. Once the results are in hand, homeowners can take action. The film reinforced this message with interviews of experts including Jane Downing, chief of the Environmental Protection Agency's New England Drinking Water Branch; Bernie Lucey, senior engineer of the New Hampshire Department of Environmental Services; Joe Ayotte from the United States Geological Survey; and scientific experts from Dartmouth.

Building on this successful model, the Dartmouth SRP is now considering producing a film about mercury, the program's other major research area. “If you choose to use a video format for research translation, it is important that you have a specific message for a specific audience and that you are giving viewers something to do to address the situation,” Rardin urged. “Conveying the message that private well owners need to protect their health by testing their water for arsenic gave us the perfect opportunity to jump into the movie-making business.”

(Angela Spivey is a contract science writer for the NIEHS Superfund Research Program.)

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Interdisciplinary experience leads to academic position

By Sophie Bolick

Rebecca Heise, Ph.D., a former trainee at NIEHS, is taking the next step in her scientific career this semester as a tenure-track assistant professor in the Biomedical Engineering Department at Virginia Commonwealth University. As a freshly minted Ph.D. in bioengineering, she joined the Matrix Biology Group in the NIEHS Laboratory of Respiratory Biology (LRB) in August 2008, where she took an interdisciplinary approach to lung injury research during her two years as a postdoctoral fellow.

Building upon her past research experience studying mechanical stress in the bladder, her work on ventilator-induced lung injury (VILI) sought to understand the mechanisms by which lung cells sense and respond to mechanical strain. According to Heise, this is an important area of research because mechanical ventilation can cause or worsen lung injury, although respirator support can be crucial for a patient's survival. In some cases, VILI can even lead to respiratory failure and death.

Combining engineering and molecular biology

Working with NIEHS Principal Investigator [Stavros Garantziotis, M.D.](#), Heise showed that mechanical stress of alveolar epithelial cells causes epithelial-to-mesenchymal transition (EMT) via production of hyaluronan, an extracellular matrix protein, and activation of the innate immune response. This work was recently accepted for publication in the *Journal of Biological Chemistry*. She plans to continue this area of research at VCU.

Heise was drawn to working with Garantziotis because it was an opportunity to build upon her engineering expertise and learn a new skill set. She acknowledged that she “will have more of a background in molecular biology than most engineers.” Garantziotis credits her hard work for her successful job search. “She was able to build on skills she had developed as a Ph.D. student, while applying them in a different model,” he said. “This [skill set] enabled her to have a running start, but also allowed her to claim novelty in her approach.”

“Stavros has been very helpful in giving me opportunities to collaborate with others and pursue my own research interests, but also keeps the focus on the big picture,” Heise said of Garantziotis’ support and mentoring. In comparing her graduate experience in a much larger lab to her experience at NIEHS, she commented, “There is an advantage to being in a smaller lab.”

Capitalizing on fellowship resources

In preparing for an academic career, Heise took advantage of the numerous resources afforded fellows at NIH. She was a regular attendee at career development workshops offered by the [Office of Fellows’ Career Development \(OFCD\)](#) at NIEHS, as well as those made available by the Bethesda-based NIH Office of Intramural Training and Education. She relied on both NIEHS OFCD Director Diane Klotz, Ph.D., and NIEHS Deputy Scientific Director Bill Schrader, Ph.D., for helpful advice during her job search, from preparing for her interview to negotiating her start-up package.

Heise was active in the NIEHS fellows’ community, serving as a member of the [NIEHS Trainees Assembly](#) steering committee and NIEHS Annual Career Fair planning committee. She also represented NIEHS at the monthly meetings of the NIH Fellows Committee.

Heise holds dual undergraduate degrees in biomedical and chemical engineering from Carnegie Mellon University. She earned a Ph.D. in bioengineering from the University of Pittsburgh. She said she was drawn to VCU because of the strong collaborations the engineering department has with the medical school. “It’s all about the fit with the department you’re applying to,” she added.



With planning, solid mentoring, utilization of resources, and networking, Heise took control of her fellowship experience at NIEHS. (Photo courtesy of Steve McCaw)



With his dual role as a principal investigator in the LRB and as medical director of the Institute’s Clinical Research Unit, Garantziotis was an ideal mentor for Heise. (Photo courtesy of Steve McCaw)

(Sophie Bolick, Ph.D., is a postdoctoral fellow with the Molecular and Genetic Epidemiology Group in the Laboratory of Molecular Carcinogenesis.)

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Dartmouth researcher receives Superfund award

By Marisa Naujokas

Courtney Kozul-Horvath, Ph.D., is the thirteenth recipient of the annual [Karen Wetterhahn Memorial Award](#). The award was presented on Nov. 12, at the 2010 NIEHS Superfund Research Program (SRP) Annual Meeting hosted by Oregon State University in Portland. The SRP recognized Kozul-Horvath for her contributions to research on effects of low dose arsenic exposure on the immune system.

Kozul-Horvath is a postdoctoral fellow in lab of Richard Enelow, M.D., at Dartmouth Medical School. She earned her B.A. from Regis College and was valedictorian in 2006. She earned her Ph.D. in 2009 under the direction of SRP grantee Joshua Hamilton, Ph.D., in the Program in Experimental and Molecular Medicine at Dartmouth.

Kozul-Horvath has studied effects of low dose arsenic exposure in drinking water on the immune system in adult and developing mice. Arsenic is a major health concern in the U.S. and worldwide. Arsenic is present in a large portion of Superfund sites and occurs naturally in rock formations.

Her Ph.D. thesis research was the first to demonstrate that arsenic exposure can increase susceptibility of mice to sublethal doses of influenza virus. Arsenic-exposed mice showed increased susceptibility and severity of respiratory influenza infection as a result of a compromised innate immune system.

The results of her research attracted attention from the scientific community and the mainstream media, including public radio. She used the opportunity to reach out to the public and raise awareness about arsenic exposure. She is continuing this research as a postdoctoral fellow, focusing on immunological effects in offspring after maternal exposure during pregnancy in mice.

Kozul-Horvath credits SRP for offering a rigorous research environment where she continues to explore issues fundamental to the understanding of how toxicants disrupt human health. She is often reminded of other research disciplines that also contribute to this understanding. She values the interdisciplinary approach supported by SRP during her training, and plans to continue to integrate this approach into her future research.

Karen Wetterhahn, Ph.D., was a chemistry professor at Dartmouth College and the founder of the Dartmouth Toxic Metals Superfund Research Program. Shortly after her tragic death in 1997, NIEHS began presenting an award in her memory to recognize an outstanding graduate student or postdoctoral researcher who best exemplifies the qualities of scientific excellence exhibited by Wetterhahn herself.

(Marisa Naujokas is a contract employee with the NIEHS Superfund Research Program and Worker Education and Training Program)



Kozul-Horvath, above, is shown in her lab at Dartmouth. Her Wetterhahn Award provides support for her to attend one major scientific conference, in addition to travel funds for attending the SRP Annual Meeting where she presented her research. (Photo courtesy of Courtney Kozul-Horvath)

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Science Notebook

Researchers honored at Science Awards Day

By Ernie Hood

NIEHS Intramural scientists and trainees stepped away from their laboratories and devoted the day to recognizing the scientific achievements of their colleagues and peers at the eighth annual NIEHS Science Awards Day Nov. 4.

The event was sponsored by the NIEHS [Office of the Scientific Director \(OSD\)](#), and was organized and moderated by Special Assistant to the Scientific Director Joel Abramowitz, Ph.D., who set the tone for the day in his letter of welcome to attendees. Abramowitz wrote, “Often science is done by groups, and often we cloak ourselves in collective anonymity. Here today we hope to give the Institute’s best workers a place in the sun.”

The award winners themselves shared that place in the sun, along with 94 trainee posters vying for Best Poster Presentation honors in three categories and nine trainee presenters seeking recognition for Best Oral Presentation ([see text box](#) for the full list of award winners).

Awards ceremony talks

Following welcoming remarks by NIEHS/NTP Director Linda Birnbaum, Ph.D., and Abramowitz, Outstanding Staff Scientist winner [Jane Hoppin, Sc.D.](#), of the Epidemiology Branch, presented an overview of her research, “Pesticides and allergic outcomes in farming adults.” Since joining the Institute in 1999, she has been a co-principal investigator of the Agricultural Health Study, a prospective study of licensed pesticide applicators from North Carolina and Iowa originally recruited in 1993-1997 ([see story](#)). In her presentation, she described how data from the study has shown that growing up on a farm could have a protective effect against allergic diseases such as asthma and rhinitis, but that the evidence also suggests that applying pesticides can reduce that protective effect and increase disease susceptibility.

The day featured morning and afternoon sessions devoted to oral presentations and poster presentations, after which attendees heard from Early Career Award winner [Xiaoling Li, Ph.D.](#), from the



NIEHS Director Linda Birnbaum was on hand to welcome attendees and praise the scientific excellent of the Institute’s senior scientists and trainees whose contributions are celebrated on the first Thursday of November each year. (Photo courtesy of Steve McCaw)



Outstanding Staff Scientist Jane Hoppin described her work involving pesticides and allergic outcomes in farming adults. (Photo courtesy of Steve McCaw)

Laboratory of Signal Transduction, who elaborated on her work examining the central role the gene *SIRT1* plays in the aging process, metabolic diseases, and the impact of environment factors on aging. In her summary of her work over the last four years, she noted that the sirtuin family of proteins, regulated by *SIRT1* and the other sirtuin genes, “could be therapeutic targets for diseases of aging or aging itself.”

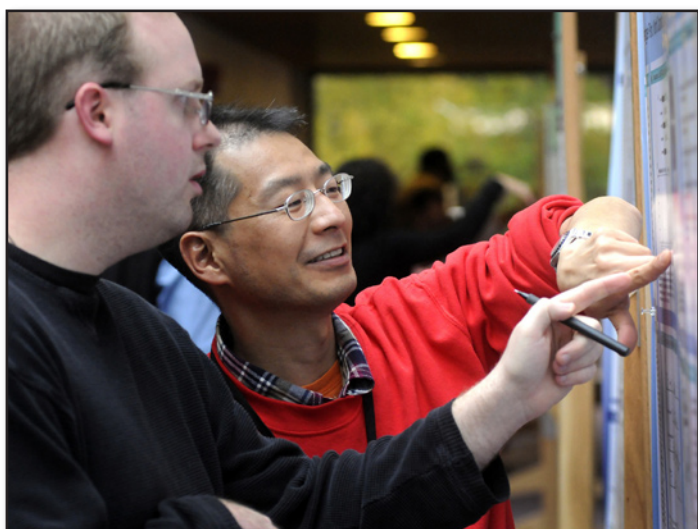
Next, Acting Scientific Director David Miller, Ph.D., presented the prestigious Scientist of the Year award to [Dale Sandler, Ph.D.](#), who has been with NIEHS since 1979 and has served as chief of the Epidemiology Branch since 2004. Quoting from one of the letters nominating Sandler for the award, Miller said, “Sandler’s work has been characterized as a major catalyst in the evolution of epidemiology, [with] seminal contributions across the field of epidemiology through publication of important papers on chronic renal disease, cancer, cardiovascular disease, and breast cancer.”



Li, left, accepted the Early Career Award from Miller. Li was also a co-author of the Paper of the Year with her Laboratory of Signal Transduction colleagues. (Photo courtesy of Steve McCaw)



NIEHS Trainees Assembly representative Sindura Ganapathi, Ph.D., left, congratulated the group’s Mentor of the Year selection, Matthew Longley of the Laboratory of Molecular Genetics. (Photo courtesy of Steve McCaw)



Research Fellow Yukitomo Arao, Ph.D., of the Laboratory of Reproductive and Developmental Toxicology, right, discussed his group’s poster with Brant Hamel, Ph.D., a postdoctoral fellow in the NIEHS Molecular Endocrinology Group. (Photo courtesy of Steve McCaw)



Scientist of the Year, Epidemiology Branch Chief Dale Sandler, described the contributions of epidemiological research to advancing the environmental health sciences, including her work on the Institute’s major large-cohort, longitudinal studies. (Photo courtesy of Steve McCaw)

Sandler presented an overview of the work encompassed in her distinguished career, which has included the establishment of large, scientifically fruitful cohorts such as the Agricultural Health Study and the 50,000-woman Sister Study, which examine breast cancer risk. With that backlog of experience, she was recently named principal investigator of the GuLF (Gulf Long-Term Follow-up) Study, a large prospective health study of oil spill cleanup workers and volunteers ([see story](#)).

Sandler is the first woman and the first epidemiologist to be recognized as the NIEHS Scientist of the Year. 2010 is the first year that the Science Awards Day proceedings were webcast for the benefit of those unable to attend in person.

(Ernie Hood is a contract writer for the NIEHS Office of Communications and Public Liaison.)

And the winners are...

Scientist of the Year — Dale P. Sandler, Ph.D., Epidemiology Branch

Early Career Award — Xiaoling Li, Ph.D., Laboratory of Signal Transduction

Outstanding Staff Scientist — Jane A. Hoppin, Sc.D., Epidemiology Branch

Mentor of the Year — Matthew J. Longley, Ph.D., Laboratory of Molecular Genetics

Best Poster Presentation in Environmental Biology — Deepti Dwivedi, Ph.D., Laboratory of Molecular Genetics, “Novel Mutator Mutants of *E. coli* NrdAB Ribonucleotide Reductase: Alterations at Allosteric Regulatory Sites and Correlation with in vivo dNTP Pools”

Best Poster Presentation in Environmental Diseases and Medicine — Ginger W. Muse, Laboratory of Molecular Carcinogenesis, “RNA Pol II Pausing Plays a Critical Role in the Mammalian Inflammatory Response”

Best Poster Presentation in Environmental Toxicology — Kalina Rangelova, Ph.D., Laboratory of Toxicology and Pharmacology, “Formation of Highly Reactive Sulfite-derived Free Radicals by the Activation of Human Neutrophils”

Best Oral Presentation — Jason P. Stanko, Ph.D., Cellular and Molecular Pathology Branch, “A Comparison of Mammary Gland Developmental Delays and DMBA-induced Mammary Tumorigenesis in Long-Evans and Sprague Dawley Rat Offspring Prenatally Exposed to Atrazine”

Paper of the Year — From the Laboratory of Signal Transduction: [Purushotham A](#), [Schug TT](#), [Xu Q](#), [Surapureddi S](#), [Guo X](#), [Li X](#). 2009. Hepatocyte-specific deletion of SIRT1 alters fatty acid metabolism and results in hepatic steatosis and inflammation. *Cell Metab* 9(4):327-338. [Story](#)

Selection process

The Outstanding Staff Scientist, the Early Career, the Scientist of the Year, and the Best Oral Presentation awards were selected by a group of nine extramural scientists from Triangle area universities, many of whom are NIEHS grantees. The Paper of the Year was chosen by the NIEHS Board of Scientific Counselors. Posters were judged by 54 intramural scientists. The Mentor of the Year was selected by the NIEHS Trainees Assembly.

Researchers meet to kick off nano consortium

By Thaddeus Schug

Researchers from the newly funded NIEHS nanotechnology centers gathered Nov. 15-16 in the NIEHS Rodbell Auditorium to introduce their projects and to stimulate coordination and collaboration among scientists. The meeting, “NIEHS Centers for Nanotechnology Health Implications Research (NCNHIR) Consortium Meeting,” offered an opportunity for grantees from NIEHS programs, including Nano Grand Opportunities (NanoGO), Challenge Grant, Outstanding New Environmental Scientist (ONES), and Research Project Grant (R01), to share and integrate data.

Sri Nadadur, Ph.D., the meeting organizer and health scientist administrator at NIEHS who oversees much of the Institute’s portfolio on nanomaterials in health and safety, said, “We are diving into the unknown in our investigation of nanomaterial health and safety and health implications.” Nadadur added, “The unique physical and chemical properties that make ENMs (engineered nanomaterials) so useful in the marketplace also make their interactions with biological systems difficult to anticipate and critically important to explore.”

Several speakers at the meeting underscored the critical need to investigate further the impact of these new materials on public health. ENMs represent a significant breakthrough in material design and development for medical, industrial, and consumer products. Global demand for nanomaterials and nano-enabled devices will approach an estimated \$3.1 trillion by 2015. This increased production provides increased opportunities for exposures with unknown health consequences that it is important to explore.

Gwen Collman, Ph.D., interim director of the NIEHS Division of Extramural Research and Training (DERT), opened the meeting and noted, “NIEHS has identified nanotechnology health and safety as a high priority research area.” Collman overviewed the numerous nanotechnology programs funded by DERT, as well as the in-house programs at the NTP and the NIEHS Division of Intramural Research. “We hope that this assembly of scientists can work together to push forward our understanding of nanomaterial health and safety,” she said

During their two days at NIEHS, the investigators described the aims of their projects in oral and poster presentations, and offered potential areas for data sharing and data needs. The meeting included two steering committee sessions, when members deliberated on the overall goals of the consortium. In addition, members of the External Advisory Committee (EAC) and project scientists interacted with each other. The EAC will provide input to project centers, while the project scientists will provide expertise to the centers.

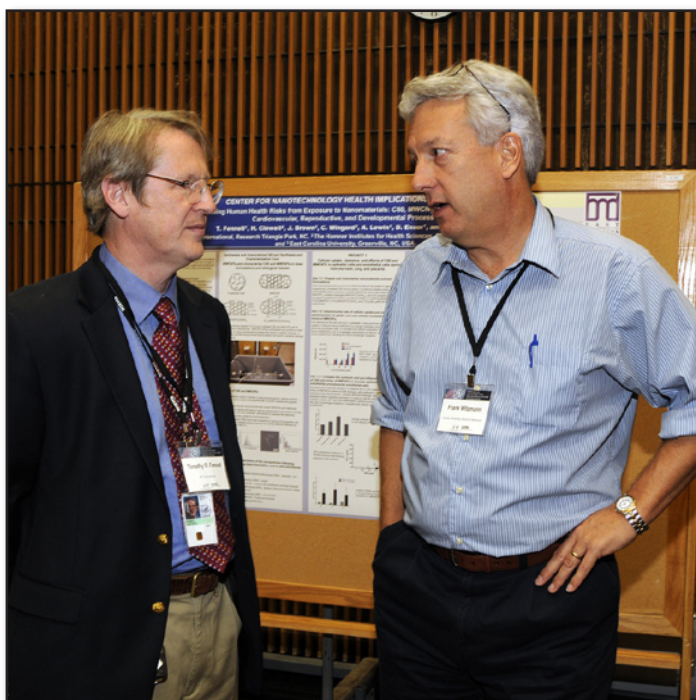


Nadadur explained how the goals of the NCNHIR consortium can accelerate understanding of the health implications and risks associated with nanomaterials. (Photo courtesy of Steve McCaw)



NIEHS Acting Deputy Director Steven Kleeberger, Ph.D., welcomed the researchers, as he pointed out the need for consortium-based research efforts to develop the wealth of data about the health and safety implications of ENMs (Photo courtesy of Steve McCaw)

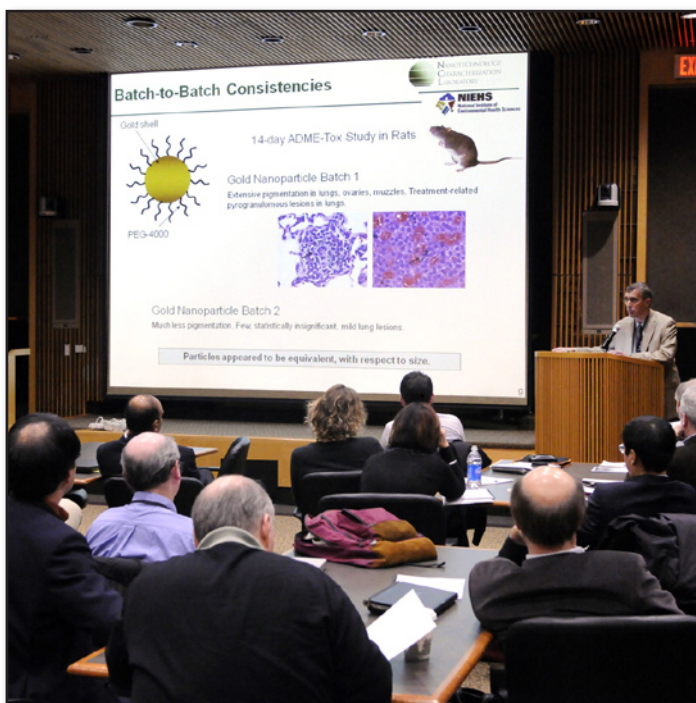
(Thaddeus Schug, Ph.D., is a postdoctoral research fellow in the NIEHS Laboratory of Signal Transduction and a regular contributor to the Environmental Factor. He is currently on detail as a program analyst in the NIEHS Division of Extramural Research and Training.)



RTI International center director Timothy Fennel, Ph.D. (left), discussed nanomaterial health and safety with NanoGO grantee Frank Witzmann, Ph.D., from the Indiana University School of Medicine. (Photo courtesy of Steve McCaw)



DETR Program Administrator David Balshaw, center, and University of Southern California center director Jim Zhang, Ph.D., right, listened to presentations by project scientists. Balshaw oversees several NIEHS-funded projects involving the development and testing of nanotechnology-based personal exposure sensors. (Photo courtesy of Steve McCaw)



NIEHS nano grantees looked on as Scott McNeil, Ph.D., from the National Cancer Institute, explained how the Nanotechnology Characterization Laboratory will provide support and expertise to the consortium. (Photo courtesy of Steve McCaw)



Consortium scientists Andrew Maynard, Ph.D., left, from The University of Michigan, and Anita Lewin, Ph.D., from RTI International exchanged ideas on nanomaterial health and safety. (Photo courtesy of Steve McCaw)

NIEHS Centers for Nanotechnology Health Implications Research Consortium (NCNHIR)

By Matt Goad

NIEHS has awarded approximately \$9 million per year in grants and support over five years to study the health risks associated with ENMs. The funds will support a nano consortium consisting of five NCNHIR research centers and three smaller projects for detailed study of ENMs and their health implications. The funds also establish partnerships with the National Cancer Institute's Nanotechnology Characterization Lab (NCL) and the National Institute of Biomedical Imaging and Bioengineering (NIBIB).

NCNHIR Research Program Cooperative Agreement (U19) Centers

- The RTI International Center for Estimating Human Health Risk from Exposure to Nanomaterials will focus on the effects of carbon-based nanomaterials. Director – [Timothy Fennell, Ph.D.](#)
- At the University of Washington, researchers will assess the risks of Qdots, luminescent semiconductor nanocrystals composed of heavy metal cores. Director – [Terrance Kavanagh, Ph.D.](#)
- The University of California Los Angeles Center for Nanobiology and Predictive Toxicology will study how metal, metal oxide and silica nanoparticles may play a role in pulmonary toxicity. Director – [Andre Nel, M.D., Ph.D.](#)
- Pacific Northwest National Laboratory (PNNL) Center for Nanotoxicology that will develop an understanding of how nanomaterials interact with biological systems. Director – [Joel Pounds, Ph.D.](#)
- University of Southern California researchers will study the respiratory effects of silver and carbon nanomaterials, focusing on the lung lining fluid. Director – [Jim Zhang, Ph.D.](#), who recently moved from the University of Medicine and Dentistry of New Jersey

Three individual five-year Research Cooperative Agreements (U01):

University of California-Davis, co-principal investigators – [Laura Van Winkle, Ph.D.](#), and [Kent Pinkerton, Ph.D.](#); University of Michigan, Principal Investigator [Martin Philbert, Ph.D.](#); New York University, co- Principal Investigators [Lung-Chi Chen, Ph.D.](#), and [Terry Gordon, Ph.D.](#)

Two two-year collaborations

NIEHS is partnering with the NCL to characterize ENMs used in risk and hazard studies and NIBIB to develop an extensive nano registry.

(Matt Goad is a contract writer with the NIEHS Office of Communication and Public Liaison.)

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Nel delivers nano lecture

By Thaddeus Schug

“Nanomaterials are increasingly coming into contact with people and the environment, and understanding how they interact with biological systems is essential to ensure their safe use,” maintains NIEHS grantee Andre Nel, M.D., Ph.D. Nel, who is a Professor and Chief of NanoMedicine at the University of California, Los Angeles (UCLA), spoke on “Nanotoxicology as a Predictive Science: From Cells to Whole Animals,” at the Keystone Science Lecture Seminar Series Nov. 17.

Nanotechnology has been a rapidly developing field over the past decade, but very little research exists about how the tiny particles may impact human health and safety. “Nanotechnology and engineered nanomaterials (ENMs) have led to rapid advancements in medicine, engineering, and biotechnology,” said Nel.



Nel is director of the Center for the Environmental Impact of Nanotechnology and the NIEHS-funded Center for Nanobiology and Predictive Toxicology, both of which are based at UCLA. (Photo courtesy of Steve McCaw)

“The challenge for us is to use [lessons from] the problems encountered through the use of industrial chemicals to prevent environmental health and safety problems from the implementation of nanotechnology. This is an enormous challenge because of the rapid pace of nanotechnology development,” Nel added.

Nel explained how he and his colleagues at The Center for Environmental Implications of Nanotechnology (CEIN) as well as the Center for Nanobiology and Predictive Toxicology at UCLA investigate how a range of potentially new properties such as size, shape, structure, and reactive surface may influence ENM behavior in biological systems.

“We use a systems biology approach to understand how this wide range of properties at the level of molecules and cells could lead to adverse biological responses that may predict their impact on human health and more complicated organisms in the environment,” Nel explained.

Developing a predictive science for nano safety

According to Nel, the novel size and unique chemical and physical properties of nanomaterials provide for an endless number of biological integrations. To deal with these complexities, Nel and his colleagues have been developing sophisticated high-throughput screening technology that allows for high capacity data generation.

“The idea is that we can use predictions, coming from these studies to identify those materials that could pose a hazard in humans and more complicated life forms in the environment, to allow us to prioritize *in vivo* testing, which cannot serve as the primary test platform due to cost and time,” said Nel.

Nel utilizes an organized workflow plan, which he referred to as the “key ingredients needed to establish a predictive science at the nano-bio interface.” The first phase is to synthesize nanomaterial libraries with unique properties and to develop detailed characterization of those materials and their properties using technology such as electron microscopy, x-ray diffraction analysis, zeta potential and dynamic light scattering.

Next, they develop and implement the appropriate biological assays and computational analyses needed to predict and rank hazard potential through cellular high throughput screening before prioritizing which materials should be tested in animal systems. Finally, these predictions are validated in whole animal systems (see text box).

Nel concluded his talk by saying, “Because of the relative lack of knowledge of these new materials and the potential adverse effects on human health and safety, now is the opportune time to launch the research and decision-making tools to ensure safe implementation of this new scientific field.”

“Andre is really at the forefront of developing *in vitro* modeling systems that can be effectively used to screen and predict for potential harmful effects of nanomaterials,” Sri Nadadur, Ph.D., a health scientist administrator in the NIEHS Division of Extramural Research and Training, and organizer of the lecture. Nadadur added, “We are excited to have Andre’s expertise in predictive modeling as part of our newly-funded nano consortium ([see story](#)).

(Thaddeus Schug, Ph.D., is a postdoctoral research fellow in the NIEHS Laboratory of Signal Transduction and a regular contributor to the Environmental Factor. He is currently on detail as a program analyst in the NIEHS Division of Extramural Research and Training.)

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Proof of principle for a predictive modeling system

Nel described experiments his group conducted to determine toxicity of nanoscale metal oxides. Following detailed characterization and performance of *in vitro* assays, materials posing toxicity were tested in zebrafish embryos and in rodents, which underwent pulmonary exposure. Nel presented data showing that the major classes of metal and metal oxides that pose danger at the cellular level also exert effects on hatching success, survival, and the development of morphological abnormalities in zebrafish, as well as generation of pulmonary inflammation in mice.

Nel showed how the observations made during *in vitro* experiments correlated with, and deviated from, those shown in the whole animal. The data illustrate that it is possible to use *in vitro* hazard ranking as determined by heatmaps and self-organizing maps and to test those predictions in whole animals with some measure of success, but also demonstrate differences in the behavior of mammalian cells and zebrafish in their response to nano-silver.

Environmental Mutagen Society highlights Wilson’s research

By Jeffrey Stumpf

The 41st annual meeting of the [Environmental Mutagen Society \(EMS\)](#) Oct. 23-27 in Fort Worth, Texas showcased the importance of NIEHS to the environmental health community.

NIEHS Principal Investigator [Samuel Wilson, M.D.](#), head of the DNA Repair and Nucleic Acid Enzymology Group, received the group’s top award for his national leadership in environmental health sciences. The society recognized Wilson’s lifetime achievement for groundbreaking fundamental studies on the mechanisms and biology of base excision repair and DNA polymerases.

“I am extremely honored to receive this award from the society that very closely mirrors the range of research and outreach programs sponsored by the NIEHS/NTP,” Wilson said at the award ceremony. “This is work I am very proud to have conducted at NIEHS over the past 15 years.”

In addition, the conference recognized research performed in the [NIEHS Mitochondrial DNA Replication Group](#) headed by Principal Investigator Bill Copeland, Ph.D. Visiting Fellow Rajesh Kasiviswathan, Ph.D., received an EMS travel award, while the mitochondrial mutagenesis platform leader chose postdoctoral fellow Jeffrey Stumpf, Ph.D., to provide an abstract talk on the group's study, "Evidence That MtDNA Depletion But Not Point Mutations or Deletions Causes DNA Polymerase-related Mitochondrial Disease."

The National Toxicology Program reported on studies managed by Kristine Witt of the [Biomolecular Screening Branch](#) on the mutagenicity of herbal products and the genotoxicity of the chemotherapeutic agent hydroxyurea. Witt also co-authored a poster with FDA colleagues that presented an evaluation of the relationship between specific genotoxicity testing results and rodent tumor induction.

In her role as co-chair of the Special Interest Group, Women in the EMS, Witt chaired the final plenary lecture of the meeting given by [Julie Ross, Ph.D.](#), an epidemiologist at the University of Minnesota Masonic Cancer Center. Ross described her work in the epidemiology of childhood cancer that makes use of interdisciplinary studies to understand and characterize the environmental and genetic factors involved in development of infant leukemias.

Funding and mentorship by NIEHS is pivotal to EMS

The EMS community is comprised of scientists from the National Toxicology Program along with the divisions of intramural and extramural research. Through its extramural research program, the NIEHS awards grants to many of the EMS members.

NIEHS Program Administrator Daniel Shaughnessy, Ph.D., explained, "Both the EMS and NIEHS are interested in mechanisms of mutagenesis, environmental stressors that affect epigenetic regulation, toxicant-induced effects on mitochondrial function, and the contribution of environmental exposures to human health and disease."

The extramural research program also emphasized the training and mentoring aspects of its mission at the EMS meeting. Superfund Research Program trainee [Senthilkumar Perumal Kuppusamy](#) from the University of Iowa earned the Alexander Hollaender Student Travel Award for outstanding research by a student from a developing country.

"A large emphasis in the EMS mission is mentoring students and helping new investigators," noted Shaughnessy. "EMS meetings have a strong educational and outreach component, including travel awards and talks for students and postdocs."



Wilson presented his award lecture, "Base Excision Repair and Environmental Mutagenesis," at the Oct. 26 EMS Award Banquet. In addition to his distinguished scientific career at NIEHS, Wilson carried executive responsibilities as the Institute's deputy director from 1996 to 2007 and acting director from 2007 to 2009. (Photo courtesy of Jeffrey Stumpf)



Shaughnessy's participation in the conference was part of an NIEHS commitment to support training and career development for students and trainees. (Photo courtesy of Steve McCaw)

The EMS society teamed up with the Federation of American Societies for Experimental Biology to provide career workshops for new investigators. Shaughnessy spoke to an audience of postdocs and graduate students about receiving the funding necessary to support a research lab. “Career developmental workshops are an important resource for postdocs and new investigators seeking training support or research funding as new investigators.”

Shaughnessy also talked about the role of program administration and other non-traditional careers in science. “Presenting a view of non-traditional scientific careers, including science writing, environmental law, and risk assessment is an important source of information for students and postdocs,” he added.

The 2011 EMS annual meeting is scheduled for Oct. 15-19, 2011 in Montreal.

(Jeffrey Stumpf, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group.)

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NIEHS hosts workshop on gut microbiome

By Eddy Ball

With its latest [state-of-the-science workshop](#), the NIEHS Superfund Research Program (SRP) took a proactive step forward Nov. 17-18 to promote an exciting new area of research in environmental health science. The purpose of the meeting was to assess existing research and explore new directions in investigating the role of the human digestive tract — or gut — ecology in health and disease, with a focus on its impact on host susceptibility and response to a wide range xenobiotic exposures.

The interdisciplinary group of scientists gathered at NIEHS to review the growing body of literature on the microbiome, the microbial communities inhabiting the human body. The scientists were particularly interested in how microbes interact with the host and environmental exposures to impair optimal health, as well as initiate or promote diseases, including cancer, in the digestive tract and elsewhere in the body.



MSU investigator and workshop organizer Norbert Kaminski, Ph.D., opened the workshop with praise for SRP's interdisciplinary emphasis and noted the growing body of literature on the involvement of the microbiome in disease processes. (Photo courtesy of Steve McCaw)

Although the gastroenterological community is becoming more keenly aware of the power of the trillions of microbes that inhabit the human gut, the ecology of the microbiome and its effects on extraintestinal disease and host gene expression remain largely uncharted — underscoring how instrumental this workshop may prove to be in advancing scientific awareness of the microbiome's role in health and disease.

In his welcome to attendees at the meeting, jointly sponsored by NIEHS and [Michigan State University \(MSU\)](#), SRP Director Bill Suk, Ph.D., linked research on the host-microbiome-xenobiotic interaction to SRP program mandates. “If we're going to be able to assess human risk and exposure leading to disease, we have to be able

to understand all of the factors and all of the cofactors associated with the host's processes. Obviously, the microbiome is a significant part of that paradigm."

The workshop began with a talk by a pioneer and leading authority in the investigation of the microbiome. Plenary presenter [Jeffrey Gordon, M.D.](#), is the director of the Center for Genome Sciences at the Washington University in St. Louis School of Medicine.

The humorous subtitle of Gordon's talk — "Dining in with trillions of fascinating friends" — set the tone for discussions of the magnitude and complexity of the landscape of the microbiome. As he explained, human intestinal microbes exceed the number of host somatic and germ cells by 10-fold, and their aggregate genome is more than 100-fold greater in size than the human genome.

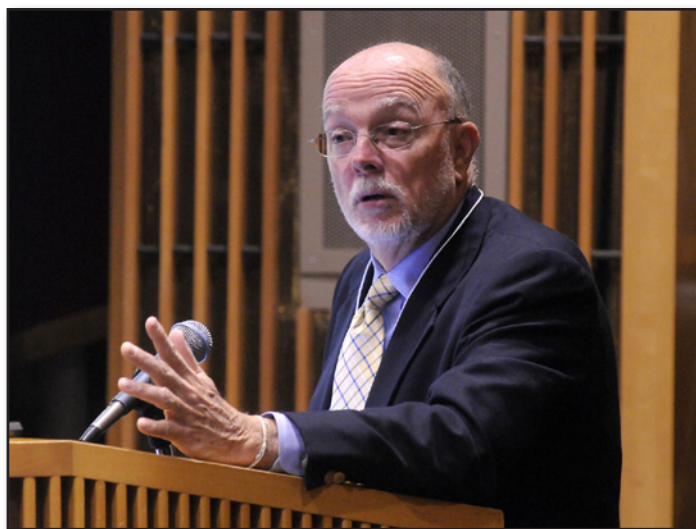
Gordon surveyed research in the field, as well as his lab's studies on the effects of fecal transplantation of microbiome samples from humans in sterile mice. In his studies, Gordon compares human samples from the United States, Malawi, and South America. Gordon is investigating the colonization patterns associated with diseases, the gene-microbiome interactions, and treatments to restore healthy microbial balance.

Following Gordon's presentation, the talks and breakout discussions that structured the workshop focused on three key questions:

- What is the state of current knowledge about the composition of the gut microbiome, and what leading edge technologies and approaches are being used to advance the science?
- How does the gut microbiome influence disease and health of the host?
- How do interactions between xenobiotics and the gut microbiome affect toxic response?

The meeting concluded with summations by breakout group facilitators and rapporteurs that understandably produced more questions than confident answers. According to organizers, workshop conclusions will be published in an upcoming paper, possibly as a commentary in the NIEHS journal *Environmental Health Perspectives*.

Despite the many unanswered questions, by the end of the workshop one thing was clear — the impact of the microbiome on human health cannot be ignored or marginalized in the promotion of public health and pursuit of effective strategies for the prevention of disease.



Suk, who was trained as a microbiologist, said he is deeply interested in the microbiome and how understanding the interrelationship with host biology and environment exposures can help answer the question of why some people are more susceptible to disease than others. (Photo courtesy of Steve McCaw)



Gordon, left, answers questions from the audience as MSU University Distinguished Professor of Microbiology and Molecular Genetics [James Tiedje, Ph.D.](#), looks on. Tiedje introduced his colleague and moderated the breakout reports. (Photo courtesy of Steve McCaw)

A diverse and impressive group of speakers

Commenting afterwards about the success of the workshop, SRP Program Analyst Beth Anderson described organizer [Norbert Kaminski, Ph.D.](#), as a “visionary [who was] responsible for the design and content of the meeting.” Kaminski, who is director of the Center for Integrative Toxicology at MSU, invited leading authorities on the microbiome whose interests and approaches reflect the breadth of interdisciplinary work in the field:

- **David Relman, M.D.**, assistant professor in the Departments of Medicine and Microbiology and Immunology at the Stanford University School of Medicine — “Stability and responsiveness of the human gut microbiota”
- **Vincent Young, M.D., Ph.D.**, associate professor in the Departments of Internal Medicine and Microbiology and Immunology at the University of Michigan — “Structure and function of the indigenous gut microbiota”
- **Gary B. Huffnagle, Ph.D.**, professor in the Departments of Internal Medicine, and Microbiology and Immunology, Pulmonary Division, at the University of Michigan — “Regulation of mucosal immunity by the indigenous microbiota”
- **Robert L. Hettich, Ph.D.**, senior research staff scientist in the Chemical Sciences Division at the Oak Ridge National Laboratory — “Integrating metagenomics with metaproteomics for comparing the molecular activities of the human distal gut microbiome in healthy vs. Crohn’s diseased individuals”
- **Patricia E. Ganey, Ph.D.**, professor in the Department of Pharmacology and Toxicology at Michigan State University — “Microbial products enhance xenobiotic-induced liver injury”
- **Arlin B. Rogers, D.V.M., Ph.D.**, assistant professor of molecular therapeutics at the University of North Carolina at Chapel Hill Lineberger Comprehensive Cancer Center — “The influence of gut microbes on extraintestinal cancers”

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Superfund researchers propose exposome paradigm

By Rebecca Wilson

NIEHS Superfund Research Program (SRP) grantees Stephen Rappaport, Ph.D., and Martyn Smith, Ph.D., published a perspective on environmental health study design in the Oct. 22 edition of *Science* magazine. In the perspective, Rappaport and Smith, who are researchers in the [University of California-Berkeley SRP](#), offer a fundamental — and possibly controversial — proposal for changing the way epidemiologists measure environmental exposure.

The article, titled “[Environment and Disease Risks](#),” presents a compelling argument that a more complete and objective picture is needed in order to help investigators discover the major causes of chronic diseases by better accounting for an individual’s total environmental exposure, or exposome.

Although current evidence indicates that environmental, not genetic, factors are primarily responsible for the risks of developing chronic diseases, Rappaport and Smith point out that epidemiologists use sophisticated genome-wide association studies (GWAS) to investigate disease prevalence while relying upon participant questionnaires to identify environmental exposures. The researchers add that the inherent inaccuracy and imprecision in questionnaire data diminish the value of detailed — and costly — genetic data and can lead to biased inferences regarding gene-environment interactions.

To remedy some of these biases, Rappaport and Smith suggest that scientists adopt the concept of the exposome to conduct the environmental equivalent of GWAS.

The exposome

Originally defined by Christopher Wild, Ph.D., director of the World Health Organization's International Agency for Research on Cancer, the exposome represents the totality of environmental exposures received by a person from conception onward. Rappaport and Smith stress that the exposome includes all toxic chemicals present in a person's internal chemical environment where disease processes originate. Evaluating the exposome is important because internal chemical environment reflects the combined effects of contaminants from air, water, and food, as well as toxic chemicals produced in the body as a result of inflammation, oxidative stress, lipid peroxidation, infections, gut flora, and other natural processes.

The authors state that peoples' exposomes can be characterized using either a top-down or a bottom-up strategy at each time point of interest. While a bottom-up strategy would entail measuring all chemicals in each external source of a person's exposure, a top-down approach would focus on all chemicals — or toxicant classes — in a subject's blood. Rappaport and Smith recommend the top-down approach because it is more efficient and would detect all toxicants in the internal chemical environment, not just those from air, water, and food. They suggest that initial studies could use archived blood samples from large prospective cohort studies for proof of concept.

Rappaport and Smith argue, "Characterizing the exposome represents a technological challenge like that of the human genome project," and the tools and technologies required to accomplish the task could well "motivate the development of commercial devices for screening important environmental exposure in blood samples." They conclude by speculating that the marriage of exposomes and genomes would lead to powerful studies able to closely examine gene-environment interactions and their role in the prevalence of chronic disease. "Such a union," they add, "might even push the nature-versus-nurture debate toward resolution."



Rappaport is director and principal investigator of the Berkeley Center for Exposure Biology, a multidisciplinary program with the goal of developing a new generation of biomarkers and biosensors for environmental epidemiology. (Photo courtesy of Stephen Rappaport)



Smith, above, and Rappaport are two of the co-directors of the Berkeley Genes and Environment Laboratory where they study the adverse effects of chemicals on human health and how genetic variation contributes to these effects and disease susceptibility. (Photo courtesy of Martyn Smith)

Summary

(Rebecca Wilson is an environmental health information specialist for MDB, Inc., a contractor for the NIEHS Superfund Research Program and Worker Education and Training Program.)

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Adelman links chromatin architecture and gene regulation

By *Negin Martin and Robin Arnette*

According to NIEHS investigator [Karen Adelman Ph.D.](#), one of the concepts that she and several other Institute researchers wanted to understand is how a cell differentially regulates two types of genes — those that only responded to specific environmental or developmental signals and the housekeeping genes that were on all of the time. Adelman's [study](#), published in the November issue of *Cell*, may have the answer, and it has to do with a gene's DNA sequence.

To learn more about Adelman's work, please see her [interview](#) on the Transcriptional Responses to the Environment Group Web page.

"If you tell me the sequence around a gene start site, we can now predict with some accuracy how that gene will be regulated and have some insights into what that gene's function might be," Adelman said.

Insight into gene regulation and its role in health and disease

Adelman's group found that many of the housekeeping genes contain a chromatin unfriendly sequence that leaves the promoter constantly open and available for expression whenever the RNA polymerase II (Pol II) arrives. In contrast, genes that shouldn't be continuously turned on — for example, those that regulate cell death — have a chromatin friendly sequence, which encourages the binding of chromatin or nucleosomes to the promoter, in lieu of the polymerase, and keeps the genes turned off. Importantly, many stimulus-responsive genes contain a paused Pol II on top of the genes' promoter site, preventing chromatin assembly and creating what Adelman calls a "musical chairs" scenario.

"When a paused Pol II is sitting on a promoter, it is poised to move into the gene and start transcription if the right cue comes from the environment, allowing for rapid gene induction," Adelman explained. "But if a polymerase isn't covering the promoter, then chromatin covers the gene, which could represses its transcription more permanently and reduce gene responsiveness to the appropriate signals."

A new way of thinking

Adelman's data indicated that if the cell needs to turn on a chromatin-covered gene, it can use chromatin remodelers to remove the chromatin and then use paused Pol II as a placeholder.



Adelman's ultimate goal is to learn how primary response genes are different from genes in other parts of the immune pathway. Doing so will allow her and others to better target the activity of these genes. (Photo courtesy of Steve McCaw)

At that point, gene activation involves triggering the release of paused Pol II, an event that can be both rapid, and finely tuned. This two-step regulation is ingrained in the DNA sequence, and the type of default chromatin structure that exists is different for genes with different fundamental functions.

Adelman said that although her group had shown that polymerase pausing is common and other researchers have examined the dependence of chromatin structure on DNA sequence, no one has previously linked these two phenomena.

“Genes that undergo pausing have their own distinct chromatin structure,” she continued. “It is a new idea because it helps you understand why these genes are regulated so differently than other genes. The work really does open the door for taking a newly discovered gene and getting insight into its regulation by looking at the DNA sequence surrounding it.”

Promising advances in immune research

Adelman performed her published studies on the fruit fly *Drosophila*, but she is now extending what she has learned into mammalian systems. Since she is interested in developmentally regulated and immune-responsive genes, she has established a system to study the inflammatory response in mouse macrophages.

Adelman’s group and others have published data suggesting that the initial wave of the inflammatory response in mammals includes a number of genes with paused Pol II. In addition, others have shown that some of these genes can be activated independently of chromatin remodeling. Thus, Adelman wants to probe the connections between the genes that can be activated independent of chromatin remodeling and genes that possess a paused polymerase.

She said, “If we can show that there are classes of inflammatory genes that have a custom chromatin structure, for instance, a class independent of chromatin remodeling and a class dependent on chromatin remodeling, then drugs that target chromatin remodelers might be designed to be more selective based on knowing the types of gene regulation employed at pro- versus anti-inflammatory genes.”

Citation: [Gilchrist DA](#), [Dos Santos G](#), [Fargo DC](#), [Xie B](#), [Gao Y](#), [Li L](#), [Adelman K](#). 2010. Pausing of RNA Polymerase II Disrupts DNA-Specified Nucleosome Organization to Enable Precise Gene Regulation. *Cell* 143(4):540-551.

(Negin Martin, Ph.D., is a biologist in the NIEHS Laboratory of Neurobiology Viral Vector Core.)

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Whole genome sequencing illuminates lagging strand DNA replication

By Jeffrey Stumpf

New research performed by NIEHS scientists may provide the answer to a decades-old question about the fundamentals of DNA replication.

The team, led by [Thomas Kunkel, Ph.D.](#), chief of the NIEHS Laboratory of Structural Biology and leader of the DNA Replication Fidelity Group, published its [findings](#) in The Proceedings of the National Academy of Sciences U S A. The work is the latest in a series of studies that determine the proteins responsible for replicating the different DNA strands across the genome.

Kunkel noted that the two strands of DNA are replicated asymmetrically, with the leading strand replicated continuously, and the lagging strand replicated slightly thereafter and discontinuously in small stretches. “The human genome encodes 15 different DNA polymerases, three of which are responsible for the vast majority of nuclear DNA replication,” he said. “The respective workload for these three polymerases has been debated for many years.”

Flags on the genome

The research group used yeast to search for the mechanism of leading and lagging strand synthesis for two major reasons. First, the various locations where replication begins, called origins, have been determined in yeast, and identification of the leading and lagging strand can be predicted. Second, yeast is easy to grow and manipulate genetically.

The authors used yeast mutants containing error-prone versions of the three polymerases that cause very specific mutations. The location of the mutations acted as flags to determine the stretch of DNA that the polymerase replicated. In addition, the mutant strains contained a reporter gene in different orientations near an origin of replication. Thus, the spectrum of the mutations in the reporter gene determines whether the polymerase error occurred on the leading or lagging strand.

These results suggested distinct roles of the major replicative polymerases, epsilon and delta. Polymerase epsilon was proposed to replicate the leading strand, while Polymerase delta (Pol delta) was proposed to replicate the lagging strand.

Last generation questions answered by next generation sequencing

Despite the elegance and clarity of the initial studies, the interpretations were based on investigations of a single origin of replication of only one of 16 yeast chromosomes, prompting the analogy of looking only under a lamp post. So, what happens in the rest of the genome?

The advent of high throughput sequencing created the opportunity to cast a light on the entire genome. Using strains that eliminate the repair of polymerase mistakes, enough mutations were present to track where the error-prone Pol delta had synthesized DNA. Near each origin, where the identification of leading and lagging strand is clear, Pol delta replicated only the lagging strand. However, closer to the middle of the origins where the two replication forks meet and either could be the lagging strand, Pol delta replicated either strand depending on the length of leading strand synthesis from each origin. As a result, this study demonstrated the probability that any region of the genome occurred by lagging strand synthesis.



Kunkel worked with current and former members of his group, as well his LMG colleagues Principal Investigator Mike Resnick, Ph.D., and Senior Staff Scientist Dmitry Gordenin, Ph.D., of the Chromosome Stability Group. (Photo courtesy of Steve McCaw)



Larrea joined Kunkel's group in June 2008 and left in May 2010. He is currently a field applications specialist with Pacific Biosciences. (Photo courtesy of Steve McCaw)

These techniques may be expanded to human cells, and Kunkel predicts further insights. “Efforts are underway to study the two other major replicative DNA polymerases, and to study how replication errors are corrected, because failure to do so contributes to cancer,” he explained.

Kunkel added, “Deep sequencing technology should provide a better understanding of how environmental stresses destabilize the genome, and may help to identify informative mutations present in cancer genomes. One can imagine a large number of applications because the whole genome is now the dosimeter to monitor cellular responses to environmental stress.”

Andreas Larrea, Ph.D., a former Intramural Research Training Award (IRTA) postdoctoral fellow in Kunkel’s [group](#), was first author on the paper. Kunkel explained that the second author on the study, IRTA Fellow Scott Lujan, Ph.D., is continuing this line of research with other members of the Laboratory of Molecular Genetics (LMG).

Citation: Larrea AA, Lujan SA, Nick McElhinny SA, Mieczkowski PA, Resnick MA, Gordenin DA, Kunkel TA. 2010. Genome-wide model for the normal eukaryotic DNA replication fork. *Proc Natl Acad Sci U S A* 107(41):17674-17679.

(Jeffrey Stumpf, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group.)

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This month in EHP

By Melissa Kerr

The December issue of [Environmental Health Perspectives \(EHP\)](#) heats up with the feature news article “A Closer Look at Climate Change Skepticism,” which discusses how media portrayals of the debate over climate change often miss the mark when it comes to specific areas of scientific disagreement. A second news feature turns to “Cadmium Confusion: Do Consumers Need Protection?” and looks beyond the widely publicized consumer product recalls of the past year to what consumers need to know about cadmium exposure.

In this month’s [podcast](#), host Ashley Ahearn discusses potential environmental risk factors for attention deficit hyperactivity disorder (ADHD) with Susan Schantz, Ph.D., associate professor of Veterinary Biosciences at the University of Illinois at Urbana-Champaign. Schantz is an NIEHS grantee who has studied the links between ADHD and contaminants found in fish from the Great Lakes.

This issue also features the San Antonio Statement on Flame Retardants with an editorial co-authored by NIEHS/NTP Director Linda Birnbaum, Ph.D., as well as research studies and reviews including:



Second author Scott Lujan is studying the two other major replicative DNA polymerases for insights into DNA repair mechanisms linked to the development of cancer. (Photo courtesy of Steve McCaw)



<http://twitter.com/ehponline>

- ADHD: An Overview for Environmental Health Researchers
- ADHD, Lead, and PCBs: A Review
- ADHD and Polyfluoroalkyl Chemicals
- Attention in Children and Organophosphate Pesticides
- Cadmium and Carcinogenic Aromatic Amine Acetylation
- Cadmium, Blood Pressure and Hypertension: A Review
- Cadmium, Lead, and Hormones in Peripubertal Girls

(Melissa Kerr studies chemistry at North Carolina Central University. She is currently an intern in the NIEHS Office of Communications and Public Liaison.)

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Upcoming distinguished lecture by Haifan Lin

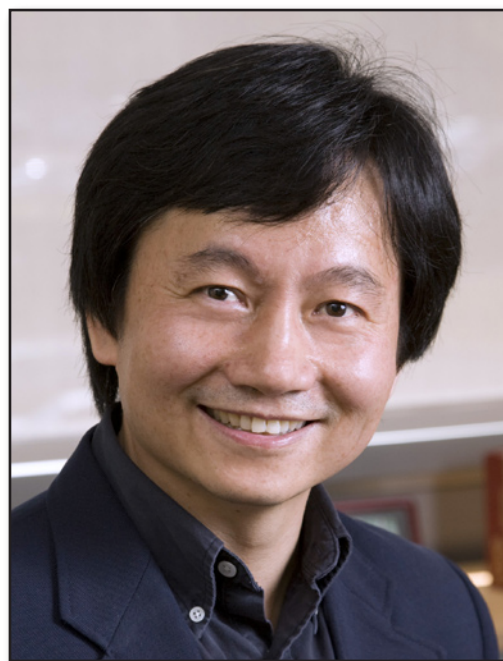
By Angelika Zaremba

NIEHS will welcome stem cell researcher Haifan Lin, Ph.D., Dec. 14 as the latest speaker in the 2010-2011 Distinguished Lecture Series. Lin will present his research findings in a lecture titled “A Novel Small RNA-Mediated Epigenetic Mechanism Related to Stem Cells,” hosted by NIEHS Principal Investigator [Guang Hu, Ph.D.](#), head of the Stem Cell Biology Group in the Laboratory of Molecular Carcinogenesis.

Lin is a professor of Cell Biology and Genetics at the Yale University School of Medicine, where he studies the mechanism of stem cell self-renewal in fruit flies, mice, and human cancer cells, and he is the founding director of the Yale Stem Cell Center. He co-founded and co-directed the Duke Stem Cell Research Program and is also a founding officer of the International Society for Stem Cell Research.

Lin’s research team studies molecular mechanisms underlying the self-renewing division of stem cells. His group is focusing on epigenetic programming and post-transcriptional regulation mediated by Piwi/Argonaute proteins and a novel class of non-coding small RNAs called Piwi-interacting RNAs (piRNAs). The piRNA complexes are involved in transcriptional gene silencing via epigenetic regulation and represent a distinct small RNA pathway that is widely thought to function only in germline.

Lin’s group is interested in the role of these molecular mechanisms in germline and embryonic stem cell division and oncogenesis. Over-proliferation of stem cells can cause cancer, whereas under-proliferation of stem cells leads to tissue dystrophy, anemia, immunodeficiency, or infertility.



Lin has received many awards and honors for his work in stem cell research. (Photo courtesy of Haifan Lin)

Lin's team discovered the Piwi protein family and was one of the first to discover piRNAs. Soon afterwards the group identified a link between the Piwi-piRNA pathway and epigenetic regulation. Based on their results, Lin's team proposed a Piwi-piRNA guidance hypothesis, in which the Piwi-piRNA complex serves as a sequence-recognition machinery that recruits epigenetic effectors such as Heterochromatin Protein 1a (HP1a) to execute epigenetic regulation.

(Angelika Zaremba, Ph.D., is a visiting postdoctoral fellow in the NIEHS Laboratory of Signal Transduction Inositol Signaling Group.)

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Extramural papers of the month

By Jerry Phelps

- [Death rates climb during heat waves](#)
- [Sequencing the exposome](#)
- [Epigenetic changes and low-dose BPA in breast epithelial cells](#)
- [Genetic driver of severe allergic asthma](#)



Read the current Superfund Research Program [Research Brief](#). New issues are published on the first Wednesday of each month.

Death rates climb during heat waves

According to research recently published by NIEHS grantees, mortality climbs during summer heat waves in the United States almost every year. These results have policy implications for addressing the burden of heat waves and for estimating the possible health effects of climate change.

According to the study, the average daily risk of non-accidental death increased 3.74 percent during the heat waves studied in 43 U.S. cities from 1987 to 2005. For each one-degree increase above average temperature, the risk of death increased 2.49 percent and 0.38 percent every day the heat wave continued. For the purposes of this study, heat waves were defined as two or more days when the average mean temperature exceeded the 95th percentile of temperatures for May through September for a given city.

Daily risk of mortality was almost double during the first heat wave of the season compared to later heat waves. The authors conclude that people were not acclimated to the heat early and may not have taken appropriate precautions such as using air conditioning or fans and curtailing outside activities. Risk of mortality was greatest in the Northeast and Midwest and the risk of death soared during catastrophic heat waves in 1995 in Chicago and Milwaukee.

Citation: [Anderson GB](#), [Bell ML](#). 2010. Heatwaves in the United States: Mortality risk during heatwaves and effect modification by heatwave characteristics in 43 US communities. *Environ Health Perspect*. Epub ahead of print. DOI 10.1289/ehp.1002313

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Sequencing the exposome

NIEHS grantees write of the need for the study of the exposome in the October 22 edition of *Science*. The word exposome was coined in 2005 and is defined as the record of all exposures, both internal and external, that individuals receive throughout their lifetime.

Martyn Smith and Steve Rappaport advocate for identifying exposures during critical windows of development. They employ the analogy of a movie trailer to explain their idea. A movie represents an individual's life and each frame of the film represents an exposure. Just as a movie trailer condenses all the important parts of the film into about 30 seconds, they believe that having a record of exposures during the important parts of our lives would be beneficial in predicting and preventing disease.

Scientists and others advocate a top-down approach using various 'omics technologies to gather information needed to understand the exposome. Their approach is to measure gene expression, protein adducts, metals, and metabolites in blood, and then use data analysis to determine which exposures are related to disease.

The idea of the exposome is gaining traction in the scientific community and in the chemical industry as well. Industry representatives think that a better understanding of exposures will exonerate many chemicals that are widely feared.

Citation: [Rappaport SM, Smith MT](#). 2010. Environment and disease risks. *Science* 330(6003):460-461.

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Epigenetic changes and low-dose BPA in breast epithelial cells

NIEHS-supported scientists at Ohio State University report that low-dose exposure of human breast epithelial cell cultures to bisphenol A causes epigenetic changes, suggesting that this model may be widely useful in studying the health effects of bisphenol A and other endocrine disruptors.

There is wide evidence that early exposure to bisphenol A and other estrogen-like compounds may increase breast cancer risk later in life. An epigenetic process has been postulated for this effect, but it is not well understood.

The researchers identified 170 genes with similar gene expression changes after the low-dose bisphenol A exposure. Further analysis revealed that the expression of the gene for lysosomal-associated membrane protein 3 was epigenetically silenced. Additional studies found the same effect in estrogen receptor alpha-positive breast tumors. The authors conclude that the combination of their exposure model, epigenetic analysis, and other assays can lead to a better understanding of the heritable effects of low-dose bisphenol A exposure in human cells.

Citation: [Weng YI, Hsu PY, Liyanarachchi S, Liu J, Deatherage DE, Huang YW, et al](#). 2010. Epigenetic influences of low-dose bisphenol A in primary human breast epithelial cells. *Toxicol Appl Pharmacol* 248(2):111-121.

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Genetic driver of severe allergic asthma

NIEHS-supported investigators at the Cincinnati Children's Hospital Medical Center have discovered a genetic basis for determining the severity of asthma. The work, carried out in laboratory mice, could form the basis for future therapeutic strategies to treat asthma.

Asthma cases have been increasing in the past few decades. The disease is triggered in susceptible people by components of air pollution, allergens, tobacco smoke, and other environmental agents.

The research team identified a pro-inflammatory protein called interleukin-17A as the chief cause of severe asthma-like symptoms in their laboratory animals. They found that exposure to allergens causes incorrect regulation of a gene called complement factor 3 that is part of the innate immune system. This results in overproduction of interleukin-17A, which in turn contributes to ever increasing inflammatory responses and hyper airway responsiveness and airflow obstruction.

The research team will continue to study the interaction of complement factor 3 and interleukin-17A in severe asthmatics, with the hope of targeting one or both of the pathways for the treatment of severe asthma.

Citation: Lajoie S, Lewkowich IP, Suzuki Y, Clark JR, Sproles AA, Dienger K, et al. 2010. Complement-mediated regulation of the IL-17A axis is a central genetic determinant of the severity of experimental allergic asthma. *Nat Immunol* 11(10):928-935.

(Jerry Phelps is a program analyst in the NIEHS Division of Extramural Research and Training.)

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Intramural papers of the month

By Erin Hopper and Robin Arnette

- [Succimer treatment shows limited efficacy at reducing organic mercury in children](#)
- [Releasing the brake on synaptic plasticity](#)
- [mtDNA helicase mutants differ biochemically](#)
- [Gender differences in glucocorticoid-mediated inflammation](#)

Succimer treatment shows limited efficacy at reducing organic mercury in children

Researchers at NIEHS recently examined the use of succimer to lower blood mercury levels in small children. Succimer is a chelating agent that the authors previously examined in the Treatment of Lead-exposed Children (TLC) trial. In the current study, the samples from the TLC trial were reanalyzed to determine whether succimer treatment was effective for treating low-level mercury exposure in children.

Organic mercury exposure comes mostly from diet, especially certain fish. Until 1999, vaccine preservatives contained organic mercury, but that source has been largely eliminated. Chelating drugs have been shown to help remove mercury from the body after an acute exposure, but these drugs have not been shown to be effective at reversing toxic effects. Research has determined that chelation does not reverse IQ deficits in lead-exposed children.

A previous effort to study the efficacy of succimer for autism spectrum disorder, thought by some to be a form of mercury toxicity, was halted due to safety concerns, so the availability of the blood samples from the TLC trial provided a unique opportunity to study succimer treatment for mercury exposure.

Blood samples collected over a period of five months were tested for inorganic and organic mercury. Succimer treatment appeared to reduce organic mercury concentrations slightly but did not reverse mercury accumulation. The authors concluded that succimer is a less effective chelator for mercury than for lead and that the modest reduction in mercury concentration that they observed is unlikely to be of clinical benefit.

Citation: [Cao Y, Chen A, Jones RL, Radcliffe J, Dietrich KN, Caldwell KL, et al. 2010. Efficacy of succimer chelation of mercury at background exposures in toddlers: A randomized trial. J Pediatr Epub ahead of print doi:10.1016/j.jpeds.2010.08.036](#)

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Releasing the brake on synaptic plasticity

A recent collaboration between NIEHS and Emory University explored the role of the protein RGS14 in brain function. RGS14 acts as a signaling protein, but its role in the brain is poorly understood. One clue to its function is that RGS14 is localized predominantly in neurons of the CA2 subregion of the hippocampus, an area that normally has very little synaptic plasticity.

To explore the role of RGS14 in brain function, the authors used a line of knockout mice that was unable to express full-length RGS14. The knockout mice appeared healthy and displayed no apparent differences in phenotype than wild-type mice. However, they exhibited a marked increase in synaptic plasticity in the CA2 subregion of the hippocampus compared to their wild-type counterparts, suggesting that RGS14 plays a role as a brake on synaptic plasticity in the CA2.

The increased synaptic plasticity observed in the knockout mice suggested that these mice may have an increased capacity for learning and memory. Indeed, the authors found that the knockout mice exhibited superior object recognition memory and an improved initial learning rate in a spatial navigation task compared to wild-type mice. These results suggest that RGS14 also acts as a brake on hippocampal-based learning and memory. Further studies are required to determine exactly how RGS14 regulates synaptic plasticity on a molecular level and what role the CA2 plays in cognition.

Citation: [Lee SE, Simons SB, Heldt SA, Zhao M, Schroeder JP, Vellano CP, et al. 2010. RGS14 is a natural suppressor of both synaptic plasticity in CA2 neurons and hippocampal-based learning and memory. Proc Natl Acad Sci USA 107\(39\):16994-16998.](#)

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mtDNA helicase mutants differ biochemically

Investigators from NIEHS performed biochemical analyses on 20 mutant variants of the human mitochondrial DNA (mtDNA) helicase gene, *C10orf2*, and determined that all of the mutants functioned properly and retained the ability to unwind DNA similar to wild-type. However, the mutants differed in their response to three other biochemical tests such as DNA binding affinity, nucleotide hydrolysis kinetics, and thermal stability. These findings will help researchers better understand mitochondrial diseases such as progressive external ophthalmoplegia (PEO), hepatocerebral mtDNA depletion syndrome (MDS) and infantile-onset spinocerebellar ataxia (IOSCA), which are caused by *C10orf2* missense mutations.

The enzyme product of *C10orf2* is known as p72, and the team members generated single amino acid substitution mutants that were identified in patients with mitochondrial disease. The researchers used *Escherichia coli* to grow the variants, many of them with changes that occurred in a linker region involved in subunit interactions and hexamer formation.

The protein purification process presented several challenges, but, through trial and error, the scientists discovered that the use of certain reagents and conditions such as a lower temperature, non-ionic detergents, elevated ionic strength, and adenosine-5'-triphosphate (ATP) cofactor in the purification buffers dramatically increased the solubility and long term stability of p72.

Team members acknowledged that their analysis of *C10orf2* proteins stressed the importance of experimental design and enzyme stability.

Citation: Longley MJ, Humble MM, Sharief FS, Copeland WC. 2010. Disease variants of the human mitochondrial DNA helicase encoded by *C10orf2* differentially alter protein stability, nucleotide hydrolysis, and helicase activity. J Biol Chem 285(39):29690-29702.

[Story](#)

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Gender differences in glucocorticoid-mediated inflammation

Research performed by scientists from NIEHS and Wake Forest University School of Medicine suggests that glucocorticoids, stress-induced steroids that regulate intermediary metabolism, may contribute to the development, progression, or susceptibility to inflammatory diseases in a gender-specific manner. This finding offers a possible explanation for why more females tend to have certain inflammatory diseases.

Using microarrays of male and female rat livers, the team discovered that glucocorticoids expanded the normal set of genes that exhibited sexually dimorphic expression. The investigators identified eight distinct patterns of glucocorticoid-regulated gene expression, which included sex-specific genes. Pathway analysis found that males had 84 additional glucocorticoid-responsive genes, which suggested the anti-inflammatory actions of glucocorticoids are more effective in males.

The authors wanted to rule out that growth hormone may be contributing to the sexually dimorphic response to glucocorticoids, so they treated isolated liver cells from male and female rats with glucocorticoids and found that the liver cells still elicited sex-specific differences in gene expression.

This work determined glucocorticoids regulate more liver genes in inflammatory pathways in males than females, suggesting that the failure by females to mount an adequate glucocorticoid inflammatory response may lead to more autoimmune diseases in women.

Citation: [Duma D](#), [Collins JB](#), [Chou JW](#), [Cidlowski A](#). 2010. Sexually dimorphic actions of glucocorticoids provide a link to inflammatory diseases with gender differences in prevalence. *Sci Signal* 3(143):ra74.

(Erin Hopper, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Structural Biology Mass Spectrometry Group.)

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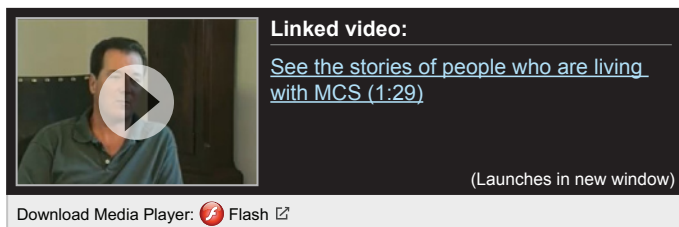
Inside the Institute

Seminar explores multiple chemical sensitivities topic

By Alicia Moore and Gerard Roman

An Oct. 27 guest lecturer at NIEHS trained the spotlight on growing concerns about Multiple Chemical Sensitivities (MCS), an environmentally triggered disability that has been linked to widespread exposures during wars in Vietnam and the Persian Gulf, as well as natural and man-made disasters, such as the BP oil spill and Hurricane Katrina.

MCS patient advocate [Alison Johnson](#), chair of the [Chemical Sensitivity Foundation](#), spoke about the condition during a seminar at the NIEHS Keystone building as part of National Disability Employment Awareness Month. The seminar was hosted by the NIEHS Disability Advocacy Committee (DAC) and co-sponsored by the NIEHS National Toxicology Program (NTP).



Johnson, above, skillfully wove statistics and personal accounts into a compelling appeal for deeper understanding of the human cost of MCS. (Photo courtesy of Steve McCaw)

In his introduction of the speaker, Steve Kleeberger, Ph.D., NIEHS acting deputy director, said Johnson's seminar was aligned with the NIEHS mission to "alleviate the burden of illness and disability," as it relates to environmental exposures.

Johnson, whose own daughter has MCS, has devoted more than 16 years of her life to the topic. Johnson has authored three books, including [Gulf War Syndrome: Legacy of a Perfect War](#) and [Amputated Lives: Coping with Chemical Sensitivity](#). She has also produced and directed a number of documentaries (see text box), including [Multiple Chemical Sensitivity: How Chemical Exposures May Be Affecting Your Health](#), [Gulf War Syndrome: Aftermath of a Toxic Battlefield](#), and [The Toxic Clouds of 9/11: A Looming Health Disaster](#).



The attendance of NIEHS Acting Associate Director Chris Long, above, and Kleeberger underscored the extent of leadership interest in helping to accommodate people with MCS at the Institute and better understand how environmental factors trigger the symptoms of the condition. (Photo courtesy of Steve McCaw)


The 1999 Consensus Definition of MCS

characterizes it as a chronic condition with symptoms reproducible with repeated exposures. Even low levels of exposure result in manifestations of the syndrome, according to the definition, and symptoms improve or resolve when the incitants are removed. Symptoms involve multiple organ systems and can be severe or even debilitating.

According to Johnson, a national random phone survey revealed that 2.5 percent of respondents said they had been diagnosed with MCS. The results suggest that more than 7 million Americans may suffer from MCS, since many sufferers may not seek medical attention or receive a diagnosis.

Johnson said recent cataclysmic events have led to an increase in the number of people with MCS. Approximately 34 percent of Gulf War veterans have MCS. Hurricane Katrina and the Gulf oil spill resulted in widespread exposures to chemicals, increasing immediate and long-term health risks for those exposed. Other exposure scenarios include the use of Agent Orange during the Vietnam War. Johnson said the incidence of MCS is growing rapidly and that it is no longer a rare condition.



There are many common MCS triggers in our environment, such as pesticides, building materials, new carpets, cleaning products, and cigarette smoke. Symptoms include headache, dizziness, muscle and joint pain, respiratory problems such as tight chest and asthma, gastric problems, extreme fatigue, and unusual memory loss.



Linked video:

[Watch the documentary \(15:00\)](#)

(Launches in new window)

Download Media Player:  Quicktime 

In June 2009, Johnson explained, the Centers for Disease Control and Prevention (CDC) established an Indoor Environmental Quality Policy for all CDC facilities. The policy prohibits scent or fragranced products at all times in all interior space owned, rented, or leased by the CDC, including use of incense, fragrance-emitting devices, wall-mounted



Laura Hall of NTP, left, talked with Johnson afterwards about her own experiences with sensitivities to certain chemicals. (Photo courtesy of Steve McCaw)

Putting a face on MCS

Johnson began her presentation with a 15-minute documentary about MCS and the people who are living with it written by Richard Starzman, and produced and edited by Johnson. The documentary demonstrates why, according to Bennie Dan Howard Sr. of the U.S. Department of Housing and Urban Development, his agency considers MCS a disability under the Fair Housing Act, Section 504 of the Rehabilitation Act — giving people with MCS protection against discrimination because of their disabilities.

A Gulf War veteran interviewed for the documentary said that once he had such a violent reaction to strong perfume that his blood pressure increased so much that emergency personnel thought he was having a heart attack — landing him in the hospital for four days. The veteran also had problems with gasoline, smoke, and cigarette odors.

An ironworker and World Trade Center first responder said the effects of exposure to chemicals in the field included burning in the nostrils, lung problems, and pneumonia. One woman interviewed had a case of MCS that left her disabled with dyslexia and learning problems with numbers and spelling.

devices, potpourri, plug-in spray air fresheners, urinal and toilet blocks, and other fragranced products. Johnson emphasized that an estimated one third of people are bothered by perfumes and that the suicide rate in the MCS community is increasing.

Johnson concluded her presentation by saying that to promote recognition of MCS is her main goal.

Following her talk, the DAC honored Johnson with an informal reception and a luncheon with DAC members. Johnson spent the afternoon at NIEHS meeting with various Institute leaders and employees.

(NIEHS biologist Alicia Moore is chair of the DAC. NIH Hispanic Employment Program Manager Gerard Roman currently serves as the NIH equal employment opportunity specialist for NIEHS.)

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NIEHS celebrates Native American Heritage Month

By L.H. Lazarus

NIEHS celebrated Native American Heritage Month this year with a lively program of historical and cultural perspectives, traditional dancing, singing, drumming, displays of tribal artifacts, and fry bread tasting. Held Nov. 17 in the NIEHS cafeteria, the event was sponsored by the Institute's Diversity Council, in collaboration with the Haliwa-Saponi Indian Tribe of North Carolina.

[Haliwa-Saponi](#) member Sharon Berrun, whose birth name is Wagetchi Tisue, narrated the program. She spoke with pride about the history of the tribe, which currently has about 4,000 enrolled members, and outlined its relationship to other Native Americans in North Carolina. The last part of the tribe's name, which means red earth, is a reference to the rich color of the soil in Eastern North Carolina. Although the state of North Carolina recognized the individuality of the Haliwa-Saponi people in 1965, the tribe is still waiting for federal acknowledgement, which it hopes to receive in the near future.

National recognition for many Native Americans has been slow in coming. It was 1990 when President George H. Bush sign congressional legislation designating November as National Native American Heritage Month. Like the Haliwa-Saponi and the Lumbee of Central North Carolina, a number of individual tribes still await official designation by the federal government.

According to Berrun, the Haliwa-Saponi cultural program was designed to help children and adults learn about and appreciate their people's heritage. Native Americans borrow traditions from each other and meld them into their regional culture. The colors in the regalia worn by each dancer symbolize the four cardinal directions and have special connotations depending on the tribe. In lieu of buckskin clothing, the Haliwa-Saponi adopted the cloth of the first colonists and decorated them with appliqué.



Dancers use the young fancy boys style for fast-paced dancing that depicts movements of the horse. Feathers are from eagle, hawk, crow, and turkey. (Photo courtesy of Steve McCaw)

“The dancers,” explained Berrun, “dance to give honor to the creator, the four winds, mother earth, grandfather wisdom, and people down through the generations.” Berrun added, “They must adapt to the sound of the drum’s tone ... to the rhythm of the beat.” Dancers tell a story “by their movements and dynamic footwork [that] replicate the movement of a horse ... of a butterfly ... trampling down grass.”

One poignant dance told of a grandfather’s dream, as he saw his granddaughter crying and cried in turn. Together their tears dripped on their clothes to become the 365 metal jingles on women’s dresses, representing each day of the year, arranged in seven rows signifying the days in a week. The regalia weigh from 25 to 50 pounds, making the dancer’s graceful movements all the more impressive to their audiences.

“Singing,” Berrun emphasized, “is an integral part of Indian culture.” Several singers harmonize on cue with a lead singer. Timing is marked with the tempo and rhythm of the drum, which she said represents the heartbeat of mother earth.

The NIEHS program ended with a friendship dance, as people from the audience joined the dancers on stage. The celebration also featured traditional Native American fry bread, a round, fried dough smothered in honey and dusted with powdered sugar — a delightful treat for everyone not overly concerned about extra calories and saturated fat.



Shown above is the traditional pecha, a mohawk-like headdress of a fancy dancer. (Photo courtesy of Steve McCaw)



The captivated audience of NIEHS staff and visitors included J. J. Bell-Nichols, right, and Elliott Gilmer, who seem almost entranced by the dancing and song taking place just a few yards in front of their seats. (Photo courtesy of Steve McCaw)



The grand entry parade showed off the dancers’ regalia, which are made by the tribe members’ families. Shown above is a male fancy dancer accompanying fancy shawl dancer Charissa Wilson, left. (Photo courtesy of Steve McCaw)

A prominent Native American at NIEHS talks about science and culture

Principal Investigator Jerrel Yakel, Ph.D., head of the Laboratory of Neurobiology Ion Channel Physiology Group, is an active member of the [Society for Advancement of Chicanos and Native Americans in Science](#). Yakel is proud of his maternal Luiseño and La Jolla heritage. Native American cultural values of “strong community ties, humility, and keeping a low profile,” he said, can make science recruiting difficult.

“Science usually requires leaving family and community,” Yakel continued, complicating the issue and possibly accounting for Native Americans being the least represented minority in science. Yakel, however, was willing to make the sacrifice. “Science fascinates me,” said Yakel, who studies nicotinic acetylcholine receptor channels in neurological disorders.

Yakel has enjoyed recognition by colleagues at the NIH, NIEHS, and professional forums for the quality of his scientific investigations. In 2008, the [American Indian Science and Engineering Society](#) profiled Yakel in an article for its magazine “Winds of Change” titled “Inspired by the Brain: Conversations with American Indian Neuroscientists,” by Cassandra Brooks.



A jingle dancer performs a medicine prayer dance that originated among the Ojibwa Nation. The hand on her hip is a feminine motion, relating to the granddaughter in the story of the jingles, while the feathers in her hand honor the creator, the four winds, and Mother Earth. (Photo courtesy of Steve McCaw)

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News from up north – the Bethesda office

By Aubrey Miller

As 2010 comes to a close, the newly rejuvenated NIEHS Bethesda office is approaching the celebration of its first full year of operation, its full complement of staff, and a long list of accomplishments.

One of the initiatives announced by NIEHS/NTP Director Linda Birnbaum when she took office in January 2009 was increase the NIEHS presence in Bethesda, because she said at the time, “Out of sight can mean out of mind.” Now, NIEHS staff in Research Triangle Park (RTP), N.C., can look back and appreciate the wisdom of her plan to raise the Institute’s visibility up north.

NIEHS has long had representation in Bethesda, specifically for Congressional liaison work headed by Mary Gant. When Birnbaum became director, however, she began expanding the office to six members who work in a variety of areas to support and advance NIEHS programs, activities, and relationships:



Chief Medical Officer and Office Supervisor Miller (Photo courtesy of Steve McCaw)

- Bethesda office manager Administrative Specialist Lindsay Lloyd, formerly a member of the NIEHS Office of the Director in RTP
- Chief Medical Officer and Office Supervisor Aubrey Miller, M.D.
- Senior Advisor for Public Health John Balbus, M.D.
- Toxicology Liaison Chris Weis, Ph.D.
- Legislative Assistant Leanna Kelly
- Legislative Liaison Mary Gant, part of the Bethesda team for more than 20 years

The broad goals of this group are to provide outreach to NIH institutes and centers and other federal agencies, academic partners, and non-governmental organizations; represent Birnbaum and other NIEHS staff at required meetings in the Washington, D.C. area, including on the NIH campus, with members of Congress, and on various interagency committees; and facilitate and coordinate certain NIEHS and NTP program areas.

Highlights of the team's productive first year

Balbus, the first new face to join the team, serves as external liaison. He has been busy on a broad range of topics and activities, including managing and cultivating the Institute's relationships with the National Academy of Sciences (NAS) and environmental health partners and supporters, and leading NIEHS efforts on the human health impacts of climate change and global environmental health. Balbus also convenes a federal liaison group to help disseminate findings from the NAS Emerging Science workshops and provide input into future activities, and functions as project officer on the Institute of Medicine Roundtable.

Along with Gant, Balbus provides a point of contact and information resource for the Friends of the NIEHS group, a coalition of non-governmental organizations and professional societies with an interest in supporting the mission of the Institute. As part of NIEHS outreach to the public health community, Balbus recently organized and moderated a special session on Social Justice, Climate Change, and Environmental Health that was led by Birnbaum. Balbus also represents NIEHS on the NIH Working Group on Global Health and the new Global Alliance for Clean Cookstoves, promoting NIEHS research and interests in these areas as well.

Miller joined NIEHS in April and immediately became involved in the Institute's multi-faceted response to the Gulf oil spill (GOS). His activities in this area include founding and co-chairing, with CDC, the federal Interagency Oil Spill Health Monitoring and Research Workgroup comprised of over 50 agency representatives, as well as testifying before U.S. Senate and House committees and partnering with NIEHS/NTP scientists and staff to develop an informational health and toxicology website to support the public health response.



Senior Advisor for Public Health Balbus (Photo courtesy of Steve McCaw)



Legislative Liaison Gant is shown speaking at a recent meeting of the National Advisory Environmental Health Sciences Council at NIEHS. (Photo courtesy of Steve McCaw)

Miller is working closely with senior NIEHS epidemiologist Dale Sandler, Ph.D., and the team as an associate investigator for the GuLF Long-Term Follow-up Study for Oil Spill Clean-up Workers and Volunteers, to develop the study protocol and meet with state and local public health officials in Gulf states to develop plans for medical referrals and implementation of the study.

August marked the arrival of Chris Weis to the Bethesda team. He immediately became involved in the GOS response, working closely with various NIEHS scientists and staff to organize and host a multi-agency meeting to address toxicological issues associated with the spill. Weis was also recently named to represent NIEHS as a co-chair on the Toxics and Risks Subcommittee of the White House Committee on Environment, Natural Resources, and Sustainability.

In 2010, Mary Gant continued to support an array of activities on the Hill related to environmental health, including testimony by Birnbaum before the Senate Committee on Environment and Public Works, the House Energy and Commerce Committee, and the Senate Committee on Veteran's Affairs. Gant has provided invaluable consultation and preparation of Birnbaum for her participation in briefings sponsored by Pew Charitable Trusts.

In her role as legislative liaison, with the capable support of Leanna Kelly, Gant also helps to ensure appropriate and successful meetings between Birnbaum and members of Congress and their staff on issues related to NIEHS research and training. As a result, 2010 has been a record-setting year for NIEHS in this regard, with the most hearings, briefings, and calls for information ever, sparking a new level of interest in NIEHS research and its results.

Last but not least, much to the regret of her colleagues in RTP, this fall, Lindsay Lloyd made the move to Bethesda, with her usual confidence and capability, and brought with her the critical administrative knowledge she's now using to support the Bethesda office operations and outreach efforts.

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*Lloyd, left, and Kelly are shown at the NIEHS Bethesda office.
(Photo courtesy of Lindsay Lloyd)*

An invitation from the staff on the Bethesda front

On behalf of all of the staff of the NIEHS Bethesda office, we are excited to be a part of the NIEHS family and look forward to better getting to know and working with our NIEHS colleagues in the coming months and years. Please feel free to contact us with questions, ideas, and opportunities in which we can integrate our efforts, and for any assistance we can offer. And lastly, we wholeheartedly invite you to please take some extra time to come by and visit with us whenever you are on the NIH campus. We're your NIEHS home away from home in Bethesda.

Warmest Regards,
Aubrey and the staff of the NIEHS Bethesda office

The Bethesda office currently occupies temporary space in Rockledge, a few miles from its permanent home in Building 31 on the NIH campus. The staff will work from its new offices for a few months, while the old office is renovated to better serve both new and visiting NIEHS staff and visitors. The temporary address is 6705 Rockledge Dr, Building 1, 8th Floor, Suite 8048.



NIEHS
National Institute of
Environmental Health Sciences

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